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OBSERVATIONS ON THE PRESENCE OF THE BACILLUS ABORTUS BOVINUS IN CERTIFIED MILK

PRELIMINARY NOTES *

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SAN FRANCISCO

A large amount of experimental work has been done during the past decade to impress on the public and profession the fact that raw milk is never a safe milk, and that in order to be fit for consumption all milk must be pasteurized. The effect has been that in many states legislation has been enacted governing and requiring the pasteurization of all milk with one exception, and this exception is certified milk. In view of the enthusiasm, entirely justified, of public health experts everywhere as to the value of pasteurization, suggestions have been rather numerous, particularly during the past two years, that even certified milk is not a safe raw product, and that it, too, should be heated. Without entering into the relative values of raw and heated milk in infant feeding, it is unquestionably permissible to say that with our present knowledge most pediatrists are still of the opinion that raw milk plays a very important and needed rôle during the first two years of life, provided such a product can be obtained as is not a potential source of danger to the infants consuming it.

It has always been the proud opinion of those medical men interested in the certified milk problem that in this product conditions as ideal as were possible had been met, and that for practical purposes certified milk was a safe raw milk. When the literature, however, began to offer suggestions here and there doubting its efficiency and safety, it became necessary for the problem to be attacked by those interested in it, in order that the foundation on which the movement had been built might be forever strengthened and its value be definitely proved, or, if it was not a dependable product, that this even more important fact should be elicited.

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* From the George Williams Hooper Foundation for Medical Research and the Pediatric Department of the University of California Medical School.

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Within certain human limitations it has always been felt by certified commissions that a very thorough safeguard had been built against the ordinary milk-borne infections due to human contamination by a fairly perfect system of dairy hygiene. The weak link in the chain, therefore, lay in that group of diseases to which man is heir, emanating from the cattle themselves. And in this group bovine tuberculosis plays the leading rôle. Tuberculin testing, performed twice a year, has succeeded in reducing the disease to a minimum, but even with this precaution some reactors are usually present, and occasionally a severe infection will decimate a herd under the best of conditions.

The following question, therefore, suggested itself. By semi-annual tuberculin tests, can we discover reactors so early in the course of their disease that they are not throwing out tubercle bacilli in their milk and in this way disseminating bovine tuberculosis? To determine this fact but one method seemed satisfactory, namely, to inject samples of certified milk into guinea-pigs in an effort to produce tuberculous lesions, if tubercle bacilli were present. A careful review of the literature has failed to show any record of this determination having ever been made with certified milk, although the number of men who have demonstrated the presence of tubercle bacilli in market milk is too large to mention. With this idea in mind, samples of certified milk were collected over a period of several months from the regular distributors so that the product as it was ordinarily consumed should be investigated.

TECHNIC

The following technic was carried out: Eight hundred cubic centimeters of milk were centrifuged for one-half hour, 2,000 to 3,000 revolutions per minute, 100 c.c. in each of eight tubes. At the end of that time the cream and skim milk were poured off and the sediments were collected in about 20 c.c. of normal saline solution. On account of centrifugalization for one-half hour, the high speed, and some experiments of one of us, it was not considered necessary to inject the cream layer, which otherwise frequently retains tubercle bacilli. Five cubic centimeters of the sediment suspended in saline were then injected intramuscularly into the upper and inner surface of the right hind thigh of a guinea-pig. Four guinea-pigs were injected for each sample of milk.

Without giving much thought to the problem when the experiments started, beyond the question as to whether or not tuberculous lesions would be discovered at the time of the necropsy, the animals in the first experiment were not disturbed for about twelve weeks. At this time two of them were chloroformed, and, as is not infrequently the case, in gathering experimental data, a very unexpected situation was discovered. The animals were not appreciably emaciated. On post-mortem examination the spleens were found markedly enlarged and studded with small grayish nodules. There was a general adenopathy, but no caseation. The testes of both animals were atrophic and the

epididymis of one contained pus. The lungs, liver and kidneys were apparently normal. Careful examination of the spleen nodules after maceration failed to show any acid-fast bacilli. We were, therefore, apparently dealing with a disease simulating tuberculosis but having its most marked effect in the spleen, lymph nodes and sex organs. The condition was immediately recognized by one of us as abortion disease of guinea-pigs, and it was evident that we had to deal with two problems, tuberculosis, for the determination of which the experiments were started, and abortion disease, the determination of which the experiments elicited.

The literature pertaining to the subject of this paper as announced in the title has been purposely not even referred to up to the present, because it seemed more logical to state first the object of the work, and then elaborate on the literature after emphasis had been laid on the peculiar manner in which our attention was focused on the positive findings.

In discussing the literature it will be desirable to consider it in the following manner: First, those investigations bearing on milk as a cause of abortion disease; second, those investigations bearing on methods of diagnosis; third, those bearing on the possible result that the presence of these organisms in milk may have on public health.

Ever since Bang,[1] in 1907, fulfilled Koch's laws in regard to the *Bacillus abortus bovinus* as the etiologic agent in abortion disease of cattle, countless investigators have been attacking the problem because of its fascinating biologic possibilities, and on account of its very great economic importance.

Theobald Smith,[2] in 1894, first called attention to a peculiar disease occurring in guinea-pigs, following the inoculation of milk, that resembled tuberculosis, but it was not until seventeen years later, in 1911, that he, in association with Marshal Fabyan,[2] determined beyond question that these lesions were due to *B. abortus*. Their conclusions at this time were:

1. *B. abortus* (Bang) is most likely the only cause of infectious abortion among cattle; 2, *B. abortus* produces in guinea-pigs a peculiar general disease that very seldom kills the animal. It resembles tuberculosis and is characterized by chronic interstitial new tissue, consisting for the most part of epithelioid and lymphoid cells; 3, *B. abortus* occurs in milk, and therefore it is indicated to determine whether it can have any causative relationship to sclerosis of tissues or organs, or to the chronic diseases of man or domestic animals.

1. Bang, B.: Die Aetiologie des seuchenhaften ("infektiösen") Verwerfens. Ztschr. f. Tiermed., Jena, 1897, **1**, 241.

2. Smith, Theobald, and Fabyan, Marshal: Ueber die pathogene Wirkung des Bacillus abortus Bang, Centralbl. f. Bakteriol. u. Parasitensk., Abt. I, 1912, **61**, 549.

Schroeder and Cotton[3] state that the udder is the favorite habitat of *B. abortus,* and in the nonpregnant cow it is the only habitat. One animal in their work showed bacilli in her milk for seven years. They injected *B. abortus* intravenously into a nonpregnant animal and the organisms disappeared in a few hours from the circulation and were present only in the udders and neighboring lymph nodes. They gave an intravenous injection to a virgin heifer 4 years old, and later the bacilli were found in the udders which had never functioned. They examined all the organs of infected animals by guinea-pig inoculation and cultural methods and found *B. abortus* only in the udders or neighboring lymph nodes, and in one instance in the pelvic lymph nodes. They assert, first, that the udders of cows are a common habitat of abortion bacilli; second, that abortion bacilli do not maintain themselves in the bodies of nonpregnant animals elsewhere than in their udders. They, furthermore, experimentally produced the disease by injecting the organisms into the udders, and call attention to the fact that milkers may perpetuate the disease by carrying it on their hands. If other workers prove their claims to be well founded, little wonder can be attached to the presence of *B. abortus* in milk. Previous to those experiments, the same investigators had examined the milk from a number of different dairies. Of 77 samples from 38 dairies, 8 samples from 6 different dairies were infected. In a second series of 140 samples from 4 dairies, Dairy A, 35 samples, showed 11 infected; Dairy B, 33 samples, 7 infected; Dairy C, 34 samples, 2 infected; Dairy D, 38 samples, 2 infected; a total of 214 samples with 30, or 14 per cent., infected.

In another series of 140 cows free from tuberculosis, the milk of nineteen was infected with *B. abortus.* In another series of thirty-six cows with a large proportion tuberculous, the milk of eleven showed *B. abortus.*

Zwick and Krage[4] isolated organisms from the milk of three cows and proved its identity by agglutination tests. They noted no changes in the udders or milk macroscopically, and concluded that *B. abortus* may pass through the udders without causing lesions. They likewise injected strains into the udders of goats and produced the disease in pregnant animals, and further injected them, both by the subcutaneous and intravenous routes, recovering the bacilli in the milk at the end of twenty-four hours, in which they were still present at the end of eight weeks' observation without demonstrable lesions in the udders.

The result of the most comprehensive, purely bacteriologic work

3. Schroeder and Cotton: The Bacillus of Infectious Abortion Found in Milk, U. S. Dept. of Agric. Rep. Bureau of Animal Indust., Circ. 216.

4. Zwick and Krage: Ueber die Ausscheidung von Abortusbacillen mit der Milch infizierter Tiere, Berl. tierärztl. Wchnschr., 1913, **29,** 41.

that has been done on milk was published by Alice C. Evans[5] in 1916. She described three groups of organisms, streptococci, staphylococci and bacilli of the abortus group. A special method of plating was necessary for isolating these bacilli, because a milk containing hundreds of thousands of *B. abortus* might pass unrecognized by the ordinary laboratory method of examination. She studied 192 samples from 161 different cows. In 45, or about 23 per cent., she discovered *B. abortus,* and in 33 of these 45, or 17 per cent. of all the samples, she isolated what she has termed the *B. abortus var. lypolyticus* on account of its fat-splitting character. Two other varieties that she isolated, B and C, resembled cultures obtained from pathogenic sources. Evans also examined by plating, two bottles of certified milk, and found that the *B. abortus* represented 25 per cent. of the total bacteria. This year, 1917, Evans[6] has reported on the further examination of the milk of 23 individual cows and the *B. abortus* developed in 17, or 73.9 per cent. The cultures of 11 samples were studied in detail, and in 9 *B. abortus var. lypolyticus* was found, while in the remaining 2, the bacilli resembled cultures from pathologic material.

The importance of the *B. abortus var. lypolyticus* has not been determined from a pathogenic standpoint.

A. Eichorn and G. M. Potter,[7] referring to them as mutation forms that morphologically and culturally resemble *B. abortus,* say that testing them against pathogenic strains by agglutination and complement fixation failed to give positive reactions. Feeding and inoculation experiments were also inconclusive. One of Evans' most interesting findings is that *B. abortus* from pathogenic sources when grown on mediums containing butter fat for nine and one-half months, has acquired a fat-splitting quality. Eichorn and Potter say that they have had several herds under observation in which abortion occurred occasionally, and in which repeated serologic tests failed to reveal the presence of *B. abortus.* Several questions are suggested to them: (1) Can it be that these fat-splitting organisms play a rôle in such cases, or are they entirely harmless? (2) Are they attenuated forms of the pathogenic variety which have lost some of their characteristics as they acquired the fat-splitting quality? (3) If this is so, may they not under certain circumstances regain their pathogenic properties? (4) Are they detrimental to human health?

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5. Evans, Alice C.: The Bacteria of Milk Freshly Drawn from Normal Udders. Jour. Infect. Dis., 1916, **18,** 437.

6. Evans, Alice C.: The Large Number of Bacterium Abortus var. Lypolyticus Which May Be Found in Milk, Jour. Bact., 1917, **2,** 185.

7. Eichorn, A., and Potter, G. M.: The Present Status of the Abortion Question. Jour. Am. Vet. Med. Assn., December, 1916, **50,** 295.

E. C. Schroeder[8] in 9 series of milk tests, injected 516 samples of milk from 90 dairies into 1,068 guinea-pigs; 103, or about 10 per cent., of the guinea-pigs developed abortus disease and the milk distributed by 29 dairies proved from time to time to be infected with abortion bacilli. He likewise fed guinea-pigs raw, pasteurized and boiled milk, and says that several of the pigs receiving raw milk developed abortion disease.

Ever since 1909, when Holth[9] and Grinstedt,[10] working independently, obtained positive agglutination tests in the serum of cattle infected with abortion disease, serum diagnosis has been generally employed in the determination of this condition. About the same time McFadyean and Stockman[11] showed the presence of antibodies in the blood of infected animals by agglutination tests.

Sven Wall,[12] after 771 examinations, concluded that the agglutination and complement fixation reactions are practical to determine infection if properly carried out. These reactions persist over six months in most animals. He infected a horse intravenously and obtained positive reactions in five days.

Hadley and Beach[13] came to the same conclusion. Brull[14] found these tests very valuable. Zwick and Zeller[15] got positive results in a very large number of cases. Larson[16] in 1912 in this country established that contagious abortion is due to the bacillus of Bang by the complement fixation test. With the exception of the English commission, all workers agree on the value of these tests on the blood

8. Schroeder, E. C.: An Experiment with Raw and Heated Cow's Milk and Its Lesson, with Comments on Bacillus Abortus, Am. Jour. Dis. Child., 1913, **6,** 334.

9. Holth, Halfdan: Die Agglutination und die Komplementbindungsmethode in der Diagnose des seuchenhaften Verwerfens der Kühe. Berl. tierärztl. Wchnschr., 1909, **25,** 686.

10. Grinstedt, P.: The Agglutination Test in the Diagnosis of Contagious Abortion of Cattle, Jour. Compar. Path. and Therap., 1910, **23,** 279.

11. McFadyean, J., and Stockman, Stewart: Epizootic Abortion in Cattle. Report of the Departmental Committee Appointed by the Board of Agriculture and Fisheries to Inquire Into Epizootic Abortion, App. to Part I, London, 1909.

12. Wall, Sven: Ueber die Feststellung des seuchenhaften Abortus beim Rinde durch Agglutination und Komplementbindung, Ztschr. f. Infektionskrankh., 1911, **10,** 23 and 132.

13. Infectious Abortion in Cattle. Jour. Compar. Path. and Therap., 1906, **19,** 191.

14. Brüll, Ziga: Beitrag zur Diagnostik des infektiösen Abortus des Rindes. Berl. tierärztl. Wchnschr., 1911, **27,** 721.

15. Zwick and Zeller: Ueber den infektiösen Abortus des Rindes. Arb. a. d. k. Gsndhtsamte., 1912, **43,** 1.

16. Larson, W. P., and Sedgwick, J. P.: The Complement Fixation Reaction of the Blood of Children and Infants, Using the Bacillus Abortus as Antigen, Am. Jour. Dis. Child., 1913, **6,** 326.

serum of infected animals. Schulz,[17] working in Dresden, in 1912 combined the agglutination test with the intradermal test. His results in the agglutination reactions are identical with those of his predecessors in the work. He found one previous record in the literature of the use of the intradermal test as a diagnostic aid, and he lays great emphasis on its value. He considers as a positive reaction any swelling on the third day of at least 5 mm. diameter. The results, however, vary with the character of the antigen used between 45 per cent. and 100 per cent.

Reinhardt and Gauss,[18] working in 1914 and 1915, report results absolutely in accord with those previously given. They worked in addition, however, with the reactions in the milk serum of infected animals with which Sven Wall had previously worked. Wall found in 25 cows, 23 reacting to blood serum tests. In 11, or about 50 per cent., the milk showed corresponding reactions. Reinhardt and Gauss, examining 27 milk serums, got positive agglutination and complement fixation tests in 21. In 15 cows, when the blood and milk were tested, they got corresponding results in 11.

To determine the time of appearance of antibodies in the blood and milk, Reinhardt and Gauss injected two goats intravenously with a culture of *B. abortus,* the first, half through her pregnancy, and the second, shortly after the birth of two kids. The first goat aborted in seven days. They got positive reactions in the blood and milk of both animals, which lasted longer and with higher dilution in Goat 1 than in Goat 2. No positive reactions were obtained with the blood of the two kids, even though they were with their mother constantly and nursed ten weeks. They conclude that in infected animals antibodies go over into the milk from the blood and last a long time.

Giltner, Cooledge and Huddleston[19] introduced pure cultures of *B. abortus* into the udders of cows and got positive milk serum tests on the following day without any evidence of gross lesions in the udders. They believe that the abortus bacillus has antigenic without pathogenic action. In every case in which *B. abortus* was found by inoculating milk into guinea-pigs, agglutinins were found in the milk, but *B. abortus* was not found in every case that gave positive tests for milk serums. Either the bacilli were present in too small numbers

17. Schulz, W.: Ueber den diagnostischen Wert der Agglutination und der Intrakutanreaktion beim infektiösen Abortus der Kühe, Inaug. Dissert., Dresden, 1912.

18. Reinhardt, R., and Gauss, G.: Untersuchungen über das Vorkommen von Antikörpern gegenüber dem Bacillus abortus infectiosi im Blut und in der Milch abortuskranker Tiere, Ztschr. f. Infektionskr. Haustiere, 1914 and 1915.

19. Giltner, Ward: Contagious Abortion. Rep. Sec. State Board Agric. and Ann. of Exper. Station, Michigan, 1911, p. 155.

to give lesions, or the presence of antibodies in the milk is a passive result from their presence in the blood of the animal.

Investigations bearing on the influence of *B. abortus* on public health have unfortunately been very few.

Mohler and Traum[20] examined the serums of forty-two persons without getting any positive complement fixation or agglutination reactions, although Larson had previously found three positive reactions in 100 serums examined. Out of fifty-six instances in which tonsils and adenoids were inoculated into guinea-pigs by Mohler and Traum, one animal showed the presence of *B. abortus bovinus*.

Larson and Sedgwick,[16] in 1913, assert that after systematically examining the serums of women who had aborted, they found that a larger number gave a positive complement fixation reaction when the *B. abortus* was used as antigen than when the ordinary syphilitic antigen was employed. They had examined, up to that time, the blood of 425 children and found seventy-three, or 17 per cent., positive and 352 negative. They also made agglutination tests which ran parallel. They concluded that the positive reactions were the result of an active immunity due to antibodies generated by the patient, and did not necessarily mean active infection of the individual. In 1915 Larson and Sedgwick[21] further report that it was observed in their original group of 425 children that those receiving milk from an abortus-free herd gave no reaction, while those fed on market milk gave a high percentage. Over 40 per cent. of the children in one institution gave positive reactions, and in one group as high as 48 per cent. reacted. In forty-two new-born children they got no reactions, but one infant in whom artificial feeding was employed on the seventh day, gave a positive reaction on the twenty-first day.

Ramsey[22] examined the blood of fifty-eight boys and an equal number of girls; six boys and one girl gave positive reactions.

Nicoll and Pratt[23] call attention to the fact that several investigators have shown that the ingestion of a large number of bacilli may give antibodies in the blood. The authors had the same results feeding guinea-pigs typhoid bacilli. In testing out a large number of infants and children in the New York Foundling Asylum with agglutination reactions, with very few exceptions they got negative results. One patient in the obstetric ward, having had a miscarriage at the seventh month, gave a positive agglutination reaction of 1 to 300, using

20. Mohler and Traum: Infectious Abortion of Cattle, U. S. Dept. of Agric., Bureau of Animal Indust., Circ. 216, 1911, p. 147.

21. Larson, W. P., and Sedgwick, J. P.: Further Studies on the Epidemic Abortion Reaction in Children, Am. Jour. Dis. Child., 1915, **10,** 197.

22. Am. Jour. Dis. Child., 1915, **10,** 201.

23. Nicoll, M., Jr., and Pratt, J. S.: Does the Bacillus Abortus (Bang) Infect Man? Am. Jour. Dis. Child., 1916, **10,** 203.

B. abortus as an antigen. Two months later her serum still gave a positive reaction 1 to 100. Her infant gave the same reaction. A fosterchild that she was nursing gave a negative reaction. The vaginal discharge, the milk of this mother and the feces of the child were injected into guinea-pigs, with negative results.

Cooledge,[24] in an effort to prove whether or not the *B. abortus* is pathogenic for man, made a number of interesting experiments. He fed 18 guinea-pigs naturally infected milk from 33 to 287 days daily (the milk being tested every four days for antibodies). Two, or 11 per cent., developed antibodies, but no lesions. There occurred 1 abortion and 2 abnormal parturitions. Two controls in noninfected milk, 2 on no milk, remained negative. Two guinea-pigs fed on negative milk, plus cultures, developed antibodies, but no lesions. There is not sufficient evidence from this experiment to warrant the conclusion that infected milk is dangerous to guinea-pigs by ingestion. It has slight antigenic, but no pathogenic, action. Fourteen normal rabbits were fed naturally infected milk for 124 days. Cooledge used 4 controls. Two were fed noninfected milk, 2 no milk. The control gave the same reactions as those receiving infected milk. Only 1 of the 14 gave an increase in antibody content during the 124 days, which persisted 84 days after stopping the feedings. There were no abortions and no postpartum lesions. Six rabbits were fed noninfected milk, plus a culture of *B. abortus;* antibodies developed to a maximum on the forty-second day, weakened on the fifty-second day and were negative in 4 of the 6 on the eighty-fourth day, although the feeding still went on. There were no abortions. The animals had two litters of young, and no postpartum lesions were evident. Infected milk is probably, therefore, not dangerous to rabbits on ingestion. It is not pathogenic, very slightly antigenic. The investigator also fed calves infected milk and got antibodies in the blood, but was not able to say whether they were due to active infection, or active or passive immunity.

Cooledge[25] examined the blood of persons drinking raw milk, pasteurized milk and no milk. Of the 6 drinking raw milk previous to the test, 3 gave positive complement fixation and agglutination tests. Of the 4 persons drinking pasteurized milk, one gave a positive complement fixation test. Those drinking no milk gave negative reactions. He then made a feeding experiment. He gave each of 7 persons 1½ pints daily for 8 weeks of a milk high in *B. abortus* and antibodies. The antibody content of the human serum was determined before

24. Cooledge, L. H.: Is Bacterium Abortus (Bang) Pathogenic for Human Beings? Jour. Med. Research, July, 1916.

25. Cooledge, L. H.: Agglutination Test as a Means of Studying the Presence of the Bacterium Abortus in Milk, Jour. Agric. Research, February, 1916, **5**, 871.

giving the milk, during the consumption, and four weeks after this period. Of the 7, 5 showed an increase in the antibody content, but in no case was this marked. He made another feeding experiment. He gave to 2 adult males daily for six weeks a negative milk, to which was added 10 c.c. of a forty-eight-hour culture of *B. abortus*. No increase in the antibody content was noted, nor were any untoward effects in evidence. Cooledge concludes:

> If the abortus antibodies in the blood were due to an infection of the individual by the organisms being present in the milk, one would expect a fairly high and lasting antibody content; but if the antibodies were due to a passive immunity, one would expect a weak reaction, persisting but a short time after stopping the ingestion of the milk. It is probable, therefore, that the antibodies represent a passive immunity due to absorption from the milk. There is very little evidence that *B. abortus* is either pathogenic or antigenic for human adults at least.

Referring to the reaction present in the blood of young children, Cooledge explains this as perhaps due to the absorption of the antibodies from the milk through the intestinal mucosa as exemplified by the work of Ehrlich and Wassermann, who found young mice capable of assimilating antitoxin through the intestinal tract and developing passive immunity to a certain degree. He does not, therefore, feel that there is sufficient proof to warrant the statement that the *B. abortus* is pathogenic to man.

EXPERIMENTAL DATA

The milk studied in our experiments was obtained from five dairies, called, for convenience, Dairy A, B, C, D and E, over a period of several months, and the number of samples examined with the dates and findings is shown in Table 1.

In order to gather some data as to the prevalence of abortus bacilli in the milk of individual cows, and at the same time to note the possible occurrence of tubercle bacilli in the milk of animals that have reacted to the tuberculin test, which six months previously had failed to react, the milk of nine recent reactors was examined, using the same technic that had been used in examining the mixed milk of the herds. The results are shown in Table 2.

Realizing that we had to deal with a condition which could only be differentiated from tuberculosis in guinea-pigs by most careful examination, a scheme was devised for studying the animals, into which the milk samples were injected, that can be best described by giving a careful history of one of the infected guinea-pigs.

TABLE 1.—DATA CONCERNING MILK SAMPLES STUDIED

Dairy	Test	Date	Guinea-Pig	Result	Percentage Positive
A	1	8/21/16	13	Negative	0
			14	Negative	
			15	Negative	
			16	Negative	
A	2	8/25/16	31	Negative	25
			32	Negative	
			33	Negative	
			34	Typ. Ab. Dis.	
A	3	9/ 2/16	55	Negative	50
			56	Negative	
			57	Typ. Ab. Dis.	
			58	Typ. Ab. Dis.	
A	4	9/23/16	59	Negative	75
			60	Typ. Ab. Dis.	
			61	Typ. Ab. Dis.	
			62	Typ. Ab. Dis.	
A	5	9/26/16	63	Typ. Ab. Dis.	75
			64	Typ. Ab. Dis.	
			65	Typ. Ab. Dis.	
			66	Negative	
A	6	10/ 2/16	71	Typ. Ab. Dis.	75
			72	Typ. Ab. Dis.	
			73	Doubtful	
			74	Typ. Ab. Dis.	
B	7	8/18/16	9	Negative	
			10	Acute Inf.	25
			11	Negative	
			12	Typ. Ab. Dis.	
B	2	8/22/16	19	Typ. Ab. Dis.	
			20	Doubtful	75
			21	Typ. Ab. Dis.	
			22	Typ. Ab. Dis.	
B	3	8/29/16	39	Typ. Ab. Dis.	100
			40	Typ. Ab. Dis.	
			41	Typ. Ab. Dis.	
			42	Typ. Ab. Dis.	
B	4	1/ 5/17	124	Typ. Ab. Dis.	100
			125	Typ. Ab. Dis.	
			126	Typ. Ab. Dis.	
			127	Typ. Ab. Dis.	
C	1	8/15/16	5	Typ. Ab. Dis.	100
			6	Typ. Ab. Dis.	
			7	Typ. Ab. Dis.	
			8	Typ. Ab. Dis.	
C	2	8/31/16	43	Negative	75
			44	Typ. Ab. Dis.	
			45	Typ. Ab. Dis.	
			46	Typ. Ab. Dis.	
C	3	9/13/16	51	Typ. Ab. Dis.	100
			52	Typ. Ab. Dis.	
			53	Typ. Ab. Dis.	
			54	Typ. Ab. Dis.	
C	4	9/28/16	67	Doubtful	75
			68	Typ. Ab. Dis.	
			69	Typ. Ab. Dis.	
			70	Typ. Ab. Dis.	
D	1	8/11/16	1	Typ. Ab. Dis.	100
			2	Typ. Ab. Dis.	
			3	Typ. Ab. Dis.	
			4	Typ. Ab. Dis.	

TABLE 1.—Data Concerning Milk Samples Studied—(*Continued*)

Dairy	Test	Date	Guinea-Pig	Result	Percent. Positive
D	2	8/23/16	23	Typ. Ab. Dis.	100
			24	Typ. Ab. Dis.	
			25	Typ. Ab. Dis.	
			26	Typ. Ab. Dis.	
D	3	8/24/16	27	Negative	75
			28	Typ. Ab. Dis.	
			29	Typ. Ab. Dis.	
			30	Typ. Ab. Dis.	
D	4	8/28/16	35	Typ. Ab. Dis.	100
			36	Typ. Ab. Dis.	
			37	Typ. Ab. Dis.	
			38	Typ. Ab. Dis.	
D	5	1/ 5/17	128	Typ. Ab. Dis.	100
			129	Typ. Ab. Dis.	
			131	Typ. Ab. Dis.	
E	1	1/ 6/17	132	Typ. Ab. Dis.	75
			133	Typ. Ab. Dis.	
			134	Negative	
			135	Typ. Ab. Dis.	
E	2	1/18/17	139	Typ. Ab. Dis.	100
			140	Typ. Ab. Dis.	
			141	Typ. Ab. Dis.	
			142	Typ. Ab. Dis.	
E	3	1/22/17	143	Negative	25
			144	Typ. Ab. Dis.	
			145	Negative	
			146	Negative	

TABLE 2.—Results of Examination of Milk of Cows Reacting to B. Abortus and to Tuberculin—Individual Cows—Tuberculin Reactors

Milk Sample	Guinea-Pig	Necropsy Findings
Dairy C, Cow 1	92	Negative
	93	Negative
	94	Negative
	95	Negative
Dairy C, Cow 2	96	Negative
	97	Negative
	98	Negative
	99	Negative
Dairy C, Cow 3	100	Negative
	101	Negative
	102	Negative
	103	Negative
Dairy C, Cow 4	104	Negative
	105	Negative
	106	Negative
	107	Negative
Dairy C, Cow 5	108	Negative
	109	Negative
	110	Negative
	111	Negative
Dairy C, Cow 6	112	Typ. Ab. Dis.
	113	Negative
	114	Typ. Ab. Dis.
	115	Typ. Ab. Dis.
Dairy C, Cow 7	116	Negative
	117	Negative
	118	Negative
	119	Negative
Dairy C, Cow 8	120	Negative
	121	Negative
	122	Typ. Ab. Dis.
	123	Negative
Dairy F, Cow 9	199	Negative
	200	Negative
	201	Negative

SAMPLE EXPERIMENT

Guinea-Pig 71. Male. Oct. 3, 1915. Weight, 272 gm. Injected intramuscularly into the inner and upper surface of right hind thigh, 5 c.c. of sediment obtained from 800 c.c. of whole milk from Dairy A, suspended in a little saline. Jan. 27, 1917, 116 days after injection, intradermal tests were made, using as antigens abortin, tuberculin, bovine, tuberculin, avian, colin, and typhoidin. Jan. 29, 1917, forty-eight hour readings were as follows:

Colin, N. P.

Abortin, 0; 3.9 by 3.9; marked edema; center yellow; necrosis.

Tuberculin, avian, N. P.

Typhoidin, N. P.

Tuberculin, bovine, 0; 0.6 by 0.6.

Feb. 2, 1917, 122 days after the injection of the milk, the animal was first injected with trypan blue for vital staining, and the dye injections were repeated daily until Feb. 24, 1917. Feb. 16, 1917, 136 days after the milk sediment was injected, the guinea-pig weighed 490 gm., a gain of 218 gm. March 5, the animal was chloroformed, 153 days after the experiment was begun. The following findings were noted:

There is a general adenopathy. The spleen, 5 by 4 cm., is enlarged and hard, contains numerous small nodules. The liver contains a few nodules. The kidneys and lungs are negative. There is an abscess in the right testicle with a firm wall. The left testicle is small and atrophic.

Bone lesions: The left ninth rib is the seat of a tumor mass, the size of a large pea, containing deep blue cheesy matter surrounded by a dense layer of tissue. The right ninth and tenth ribs are the seats of small tumors, the size of a grain. The left seventh rib at the point of insertion to the vertebra has a tumor the size of a small pea, containing cheesy matter. Spleen culture on potato glycerin serum agar, positive in eight days.

Agglutination Tests: Blood taken from the heart of the guinea-pig before chloroforming, March 15, 153 days after the milk injection, gave a positive reaction in a dilution of 1 to 1,000 to 1 to 4,000.

Recapitulating, the procedure was briefly as follows: Several weeks after the milk had been injected, intradermal tests were made, using various antigens; at this time blood was taken from the heart for agglutination determinations. Some animals were then repeatedly injected with a vital stain, following which they were chloroformed. The various organs were studied macroscopically as far as the vital staining permitted, and microscopically, and in most cases an effort was made to isolate the invading organism. The results have been carefully tabulated in a manner shown in Table 3 and the more minute details, referring particularly to cutaneous hypersensitiveness, agglutination reactions, gross and microscopic lesions and cultural characteristics of the invading organisms, will be reported in later communications.

Studying the results in detail leads to some interesting observations. Of the twenty-two samples of milk obtained from the mixed herds of five different dairies, twenty-one, or over 95 per cent., showed definite *B. abortus* infection. None showed the presence of tubercle bacilli in sufficient number to cause tuberculosis in guinea-pigs. *The*

milk of Dairy A, from which the one sample was obtained that produced no lesions, infected 50 per cent. of the animals that were injected, the experiments extending over three months. *The milk of Dairy B* infected about 80 per cent. of the animals injected, the experiments extending over a period of six months. *The milk of Dairy C* infected about 88 per cent. of the animals injected, the tests extending over a period of two months. *The milk of Dairy D* infected 95 per cent. of the animals injected, the experiments extending over a period of six months. *The milk of Dairy E* infected 66 per cent. of the animals injected, the tests having been made with only a short interval between them.

It is interesting to note that Dairy A, from which the one negative sample was obtained, was evidently a less seriously infected herd, or harbored a less virulent type of organism, than the other dairies, because in no single experiment were 100 per cent. of the guinea-pigs infected. The importance, in this connection, of using large quantities of milk and a sufficient number of animals cannot be overestimated. The quantity used, 800 c.c., is much larger than is usually recommended in the literature, and this unquestionably accounts for the large percentage of positive results. Furthermore, if fewer animals had been used in the individual tests, the results would not have been nearly as striking. In several instances the first two or three guinea-pigs were apparently uninfected, while the last animals examined were overwhelmed with the disease, showing in guinea-pigs, as in cattle, the marked individual susceptibility to the abortus bacillus.

A study of the results obtained by injecting the milk of individual cows reacting to the tuberculin test, which had not reacted to it six months before, shows that none of these animals was excreting tubercle bacilli in sufficient quantity in their milk to infect guinea-pigs with tuberculosis. About 22 per cent. of them were harboring pathogenic *B. abortus,* which corresponds fairly well with previous observations where the milk of individual cows was tested in this connection. The number tested, however, was too small to draw positive conclusions, but the result is at least suggestive.

At this point it may be well to discuss a little more in detail the methods that were used to establish a correct diagnosis in each animal, and briefly to summarize the results. The agglutination test was made according to the usual technic. Reactions under 1 to 100 were not considered positive. In the serum of the infected animals the reaction was positive in dilutions of from 1 to 600 to 1 to 1,000, and sometimes in dilutions greater than 1 to 2,000. The complement fixation test was not made because most investigators are of the opinion that the agglutination test is quite as reliable and its technic is much more simple.

The intradermal tests were always positive in infected animals, the

characteristics of the reaction being marked induration, frequently with central necrosis, an areola at least 1 cm. in diameter, with persistency of the reaction over the forty-eighth hour. The organisms were isolated in over 20 per cent. of the infected animals. In the remaining animals, either no attempt was made to isolate the organisms, or, on account of the special vital staining dye that had been injected, the bacilli did not grow on the mediums incidental to conditions the exact nature of which is being studied. By reinoculation of the spleen or isolated organisms from infected animals, the identical disease was produced in guinea-pigs. The isolated organisms were further identified by an abortus serum produced by a known *B. abortus* strain. It is of profoundest interest to note that where animals had been mated for months, infection in either the male or female practically always resulted in a failure of impregnation.

The pathologic lesions, both macroscopic, which have been referred to earlier in this paper, and microscopic will be further studied and reported in a later communication. The disease attacks principally the lymph nodes, spleen and sex organs, with a special selective action toward the last, but it may also manifest itself in the liver, bones, lungs, eyes and kidneys in some cases.

CONCLUSIONS

As far as can be concluded in a preliminary report from a limited amount of material, it may be said:

1. *B. abortus* is, for practical purposes, always present in the certified milk produced in the San Francisco Bay regions.

2. Tubercle bacilli are not present in this same milk in sufficient number to give tuberculosis to guinea-pigs, although this conclusion may prove incorrect on further experimentation.

3. If the above conclusion is correct, there is no necessity for pasteurizing certified milk on account of any danger that it may possess as a disseminator of bovine tuberculosis to infants.

4. It is not unlikely that in many previous milk tests for tubercle bacilli, the anatomic lesions of bovine abortion disease in the guinea-pig were mistaken for tuberculosis.

5. If the *B. abortus* is present in certified milk to the extent evident from these experiments, it is difficult to consider it pathogenic for infants, without, so far as is known, ever having produced recognizable lesions on post mortem examination.

6. The result of this work, however, is one more definite indication that it is of greatest importance to study the abortus problem from every angle to be absolutely certain of its bearing on the health of infants.

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TABLE 3.—Results of Intradermal Injections of Milk Sediment in Guinea-Pigs

Guinea-Pig	Sex	Weight, Gm.	How and When Injected	Time Interval, Days	Cutaneous Hypersensitiveness				Agglutination	Necropsy Findings	Cultural Results	End Weight, Gm.	Remarks
					B. Abortus Broth, 1-2	B. Abortus Protein 1-1,000	B. Typhosus Protein 1-1,000	Tuberculin bovine, glycerin 1-2 human; Alc. Precip. 1-3					
126	M	294	Milk from Dairy B, 1/5/17	54	2.8 by 2.8 M. I. R.	1.4 by 1.4	N. P.	.....	1-200 1-1,000	General lymphadenitis; spleen 3.5 by 2; scarred, nodular; testes atrophic; other organs negative.	Spleen cultures positive in 5 days	480	4/7/17, trypan blue injections begun 4/24/17, chloroformed
128	M	382	Milk from Dairy C, 1/5/17	54	3.1 by 3.4	1.6 by 1.6	N. P.	.....	1-2,000	General lymphadenitis; spleen 3.5 by 2; nodular, enclosed in inflammatory tissue from mesentery; testes atrophic; other organs negative.	Spleen cultures positive	470	3/5/17, injection of dianil blue 3/26/17, chloroformed

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THE PHENOLSULPHONEPHTHALEIN ELIMINATION IN INFANTS AND YOUNG CHILDREN *

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Since the original publication, in 1910, by Rowntree and Geraghty[1] of the results of their experimental work with phenolsulphonephthalein in determining the functional capacity of the kidney, the value of the test has received such ample confirmation as to establish it among the essentials for careful diagnosis in renal diseases.

It may be desirable to recapitulate briefly its rationale and practical limitations. No attempt has been made to cover all the literature on observations on adults, but all of Rowntree and Geraghty's publications have been consulted and enough of the more recent articles to see that their opinions are, in the main, corroborated by others.

Phenolsulphonephthalein is an ideal substance for the study of renal function, being practically nontoxic and nonirritating, readily absorbed and rapidly eliminated through the kidneys. Even the strongest advocates of indigocarmin, its nearest rival, admit the superiority of phthalein for studying the total function of both kidneys. Owing to its avidity as an acid and the production of a pure red color in alkaline solution, it lends itself readily to accurate colorimetric estimations.

From the study of a variety of experimental renal lesions in the dog, Eisenbrey[2] concludes that the phenolsulphonephthalein test is one of the most satisfactory, and, at the same time, most delicate methods of estimating the functional activity of the kidney.

Although the phenolsulphonephthalein which circulates in the blood after injection presents the same concentrations in the liver, pancreas and salivary glands as it does in the kidney, Rowntree and Geraghty[3] have shown that only a small amount of the drug appears in the bile and none in the pancreatic juice or saliva. It is clear, they believe, "that the capacity for picking out the molecules of phthalein from the infinitely dilute solution in the blood and passing them on into the

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1. Rowntree, L. G., and Geraghty, J. T.: Jour. Pharm. and Exper. Therap., 1909-1910, **1,** 579.

2. Eisenbrey, A. B.: Jour. Exper. Med., 1911, **14,** 366.

3. Rowntree, L. G., and Geraghty, J. T.: Arch. Int. Med., 1912, **9,** 284.

urinary secretion in comparatively concentrated solution, is a function specific to the kidney."

They have also obtained fairly conclusive proof that the cells of the tubules play the most important rôle in the excretion of phthalein, and that a much smaller amount must also be eliminated through the glomeruli. Furthermore, none of the usual diuretics in therapeutic doses have any appreciable effect in hastening or increasing the elimination, although, under experimental conditions, those diuretics in large doses which are believed to exert a stimulating effect on the secreting cells of the tubules, slightly increase the phthalein output.

Both from experimental and practical evidence, Geraghty and Rowntree[4] have found the intramuscular injection of a solution of phenolsulphonephthalein to be the method of choice. Elimination begins (in normal adults) in from five to eleven minutes; from 40 to 60 per cent. of the phthalein injected appears in the urine by the end of the first hour, and from 60 to 85 per cent. at the end of the second hour. Elimination is practically complete in the two hours, as only a trace appears in the third and fourth hours.

After intravenous injection, the drug appears in from three to five minutes, and from 63 to 80 per cent. is eliminated within the first hour. Subcutaneous injections result in such large variations as to vitiate their value.

In no disease, other than renal, has any very marked and consistent reduction of phthalein excretion been noted. Experimentally, Rowntree and Geraghty[3] have found a distinct reduction in very severe anemias. Straub and Bancroft (quoted by Rowntree and Geraghty[3]) have shown that in such conditions, experimentally studied, the tubular function of the kidneys may be entirely removed. This would indicate, again, that the tubules chiefly are concerned in the excretion of phthalein, but that the glomeruli are capable of excreting some of the drug. In secondary anemia, in the absence of nephritis, the output of phthalein has been found to be almost normal.

Acute Nephritis.—In acute nephritis, the capacity of the kidney to excrete can readily be determined by the phthalein test, but this means little prognostically, on account of the rapidity with which variations occur. Rowntree[5] has encountered patients who excreted only 10 per cent. of phthalein in two hours during an acute attack of nephritis, with a rise to 24 per cent. four days later. In two weeks the output had become normal. Frequent repetitions of the test, therefore, are essential for prognosis. He has never met with any instances of

4. Geraghty, J. T., and Rowntree, L. G.: Jour. Am. Med. Assn., 1916, **62**, 811.
5. Rowntree, L. G.: Am. Jour. Med. Sc., 1914, **147**, 352.

"increased permeability" in acute nephritis. Thayer and Snowden[6] note considerable reduction in the phthalein output in some instances of the cloudy swelling of the kidneys which accompanies acute infections.

Chronic Nephritis.—So far as prognosis in chronic nephritis is concerned, when the phthalein excretion is only moderately reduced, the immediate outlook is favorable, but tests should be applied intermittently to determine whether the case is stationary or progressive. The possibibity of an acute exacerbation becoming superimposed on the chronic process, necessitates caution in giving an opinion (Rowntree[5]). In general, it may be said that advanced nephritis always shows a decreased output. Thayer and Snowden[6] assert that in not a single instance of severe chronic nephritis studied within the last five years have they met with a good phthalein elimination.

On the other hand, instances of a normal output occasionally are encountered in patients with undoubted chronic nephritis. Such occurrences have been reported by Pepper and Austin,[7] and Baetjer.[8] These authors suggest that a hyperpermeability of the kidney for phthalein may exist. Thayer and Snowden consider that these cases are more or less characteristic in their clinical manifestations and are often roughly classed as chronic parenchymatous nephritis. Their most striking clinical features are the elective impermeability of the kidney to salt and the resulting tendency to hydrops. With regard to most of the other tests of function, the kidneys appear to react normally and, except for the dropsy, there may be few disturbing symptoms. As Rowntree[5] points out, the phthalein test at least furnished correct information so far as immediate prognosis in these cases of hyperpermeability is concerned, as they did not have a fatal termination while under observation. In the earlier stages of chronic parenchymatous nephritis, and in mild cases, Rowntree and Geraghty[3] find little disturbance of function, but where there is a marked decrease in phthalein elimination, marked renal changes must be present. In the presence of only traces of phthalein in the urine, or when it is entirely absent, they consider that the prognosis is grave, even though no signs of uremia exist.

In clear-cut instances of chronic interstitial nephritis, however, they find the test most valuable. Almost all such cases show more or less diminution in phthalein excretion. In all but one of twenty-two patients of this type, Brown and Cummings[9] found a parallelism between the phthalein output and the clinical symptoms.

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6. Thayer, W. S., and Snowden, R. R.: Am. Jour. Med. Sc., 1914, **148,** 781.
7. Pepper, O. H. P., and Austin, J. H.: Am. Jour. Med. Sc., 1913, **145,** 254.
8. Baetjer, W. A.: Arch. Int. Med., 1913, **11,** 593
9. Brown, Phillip King, and Cummings, W. Taylor: Jour. Am. Med. Assn., 1916, **66,** 793.

According to Rowntree,[5] it has been shown experimentally that a moderate degree of passive congestion shows a normal phthalein output, which decreases as the congestion becomes more marked, but returns to normal with the earliest signs of improvement in the circulation. Clinical confirmation of this theory is found in cardiorenal cases. Patients with moderately advanced nephritis associated with a moderate myocardial insufficiency often exhibit a fair renal capacity. An increase in the phthalein output may be the first evidence of a restoration of cardiac compensation, and hence indicates a favorable immediate prognosis. A low excretory capacity with marked increase in blood urea or total nonprotein nitrogen, indicates that the kidneys are seriously affected, or that the heart is in an extremely precarious condition. With or without "cumulative phenomena," a low excretory capacity persisting after there is clinical evidence of cardiac improvement, indicates severe nephritis and an unfavorable prognosis.

Uremia.—In eleven of sixteen patients with uremia, who died during the attack, Rowntree and Geraghty[3] found the phthalein elimination to be absent, or only a trace.

Austin and Eisenbrey[10] note that a marked decrease in elimination occurs synchronously, as a rule, with the onset of symptoms of intoxication (vomiting). Therefore, they conclude that the phthalein test would seem to be a better indication of the ability of the kidney to eliminate the toxic substances responsible for the symptoms of renal insufficiency than are the anatomic changes or the elimination of total nitrogen or chlorids.

In twenty-one cases coming to necropsy, Rowntree and Geraghty[3] found a remarkable uniformity between the phthalein output and the pathologic findings. In one patient with polycystic kidneys who died of pneumonia, the output had been normal. This corroborates the known fact that polycystic kidneys usually are found at necropsy quite unexpectedly.

In summing up the value of the phthalein test, Rowntree, Marshall and Baetjer[11] expressly stipulate that whenever the output of phthalein is decreased even but slightly, the total nonprotein nitrogen, or the blood urea, or both, should be determined. In other words, reliance cannot be placed on the phthalein test alone in the study of nephritis, no matter how valuable may be its corroborative evidence.

Comparatively few investigations in the phthalein eliminations in infants and children have been made. In 1912, before the Section on

10. Austin, J. H., and Eisenbrey, A. B.: Jour. Exper. Med., 1911, **14,** 366.

11. Rowntree, L. G., Marshall, E. K., Jr., and Baetjer, W. A.: Arch. Int. Med., 1915, **15,** 543.

Diseases of Children, R. M. Smith[12] reported a small series, as follows: Five patients with normal kidneys show from 32 to 52 per cent. elimination in one hour. The ages of the patients were not given. Fifteen patients with acute nephritis, varying in age from 3½ to 7 years, eliminated from 28 to 61 per cent. (average 44 per cent.) within one hour, and six patients with pyelitis showed an output of from 20 to 60 per cent. (average 37 per cent.) for one hour. Most of these cases of acute nephritis seem to have been mild, none proving fatal. Edema was present in nine of the fifteen. The lowest figures, 28 and 30 per cent., were found, as a rule, in the worst cases. The highest figure, 61 per cent., was found in a patient in whom the duration of the disease was not given, and who therefore may have belonged to the category of chronic parenchymatous nephritis. Another possible chronic case showed only 30 per cent. at two different tests. It must be remembered that all these figures are for one hour's excretion only, using 3 mg. of phthalein instead of 6 mm. Smith considers that the phthalein test shows the ability of the kidney to eliminate toxins and whether there is danger of uremia. It does not assist in determining the ability of the kidney to eliminate protein, salts and water.

In connection with a study of the nonprotein nitrogen and urea of the blood, Tileston and Comfort[13] estimated the phthalein output in several groups of patients varying in age from 6 months to 11 years. Only six of the patients were under 2 years of age. In five healthy children from 3 to 9 years of age, the phthalein output in two hours varied from 78 to 81 per cent. In three children with acute nephritis, from 2½ to 9 years of age, two of whom also suffered from pneumonia and scarlatina, respectively, the output varied from 39 to 54 per cent. in two hours. The figures for the remainder may be tabulated.

Disease	No. of Cases	Age	Percentage of Phthalein in 2 Hrs.
Lobar pneumonia	7	8 mos. to 9 years	45 to 85
Lobar pneumonia (Urine contained granular casts and albumin)	1	15 mos.	17
Scarlatina	8	17 mos. to 11 yrs.	49 to 86
Typhoid fever	6	3 to 10 yrs.	57 to 75
Tuberculous meningitis	2	18 mos. and 10 yrs.	79 and 55
Cerebrospinal meningitis	1	4 yrs.	78
Mixed group, pertussis, diphtheria, chorea, etc.	12	2½ to 10 yrs.	30 to 86

The authors conclude that the phthalein test is very valuable in the diagnosis of nephritis, showing probably better than any one other

12. Smith, Richard M.: Am. Jour. Dis. Child., 1913, **5,** 25.
13. Tileston, W., and Comfort, C. W.: Am. Jour. Dis. Child., 1915, **10,** 278.

method the degree of impairment of renal function. In the diagnosis of uremia and as a guide to diet, it is inferior to blood analysis, because a low phthalein output may occur without retention of nitrogen. They are also inclined to believe that the child's kidney has a better excreting capacity than that of the adult.

Leopold and Bernhard[14] also studied the nonprotein nitrogen of the blood and the phthalein output in sixty-five children.

In a group of fifty hospital patients, from 2 to 14 years of age, suffering from a variety of diseases, but free from any evidences of nephritis, the figures for phthalein excretion in two hours varied from 50 to 96, the average being 70 per cent.

The figures for the group of cases of nephritis were as follows:

Acute nephritis, 5 cases.....	23	60	69	74	85
Chronic nephritis, 5 cases.....	19	33	44	64	73
Passive renal congestion.....	38	40	42	58	78

They conclude that so far as their own cases are concerned, the figures in the nonnephritic groups are practically identical with figures obtained in adults, and that the changes in the subjects of renal disease correspond to the changes observed in adults.

Fishbein,[15] from a study of a small group of children and adults, concludes that there seems to be a general lowering of the renal function during the latter stages of scarlet fever. In nearly all uncomplicated cases in which examination was made from the third to the fifth week, a total phthalein output averaging 55 per cent. was observed, as compared with the usual figures of from 65 to 85 per cent.

Hempelmann,[16] in a study of the phthalein elimination in seven patients with orthostatic albuminuria, from 8 to 12 years of age, found an average decrease of 12.9 per cent. in the phthalein output with the patients in the position of accentuated lordosis during the test, compared with the results after a night in bed. Two normal patients showed 70 and 83 per cent. before and 71.5 and 81.8 per cent. after being in the lordotic position.

Barker and Smith[17] found normal phthalein elimination in all but one of six young male patients, from 16 to 25 years of age, suffering from orthostatic albuminuria. In three that were tested before and after standing erect for two hours, there was a slight reduction in elimination, but not enough to be of great significance.

14. Leopold, J. S., and Bernhard, A.: Am. Jour. Dis. Child., **11,** 432.
15. Fishbein, M.: Jour. Am. Med. Assn., 1913, **61,** 1369.
16. Hempelmann, T. C.: Am. Jour. Dis. Child., 1915, **10,** 418.
17. Barker, L. F., and Smith, F. J.: Am. Jour. Med. Sc., 1916, **41,** 44.

Our own studies in phthalein elimination were made on seventy-five patients in the wards of the Children's Hospital of Philadelphia, in the services of one of us (J. C. G.) and of Dr. J. P. Crozer Griffith and Dr. Alfred Hand, Jr. We take this opportunity for acknowledging our indebtedness to them.

Patients with definite renal disease were studied whenever they presented. With this exception no attempt was made at selection other than to pick out males and thus facilitate the collection of urine. The ages of the patients varied from 3 weeks to 10 years. Forty-four were under 1 year of age; seven were from 1 to 2 years, and twenty-four from 2 to 10 years. The technic was as follows:

Technic.—The older children passed urine before the test, but the infants and younger children were not catheterized at this time. The repetition of catheterization of these infants did not seem warranted. At this age, urination occurs so frequently that the amount of urine residual at the time the test was begun must have been small, in the absence of any signs of distention of the bladder. It also seems to us that the percentage of error due to residual urine in non-obstructive cases must at all times be very small. This error must be that due to the different color of the residual urine and an equal amount of distilled water, when used as a diluent, for the phthalein contained in 1,000 c.c. of the final solution (500 c.c. in our cases). The infants and younger children were held on Bradford frames, and under all the patients were placed clean, dry, cotton pads. If any urine was found to have been spilled on the pad during the test, the results were discarded. In the case of all the patients who could not voluntarily hold the urine, the penis was securely fastened in the mouth of a urinal and 0.5 c.c. of a solution containing 3 mg. of phenolsulphonephthalein (half the amount used in adults) was injected deeply into the lumbar muscles.

Catheterization with a soft rubber catheter was performed at the end of 70 minutes, or 130 minutes, or both, except in some of the older children who were able to void. The time was extended 10 minutes over the one and two hour periods to allow for the interval required for the phthalein to appear in the urine after intramuscular injection, and thus make the results comparable with those obtained after intravenous injection.

In view of the almost universal use of the intramuscular route, except in the presence of some local condition such as marked edema which would interfere, we believe it would be more desirable to allow exactly one or two hours after intramuscular injection and thus make these the standard readings. When intravenous injections are used, we would have different figures for the standard.

At the end of the time allowed, the urine passed, and that obtained by catheter was alkalinized with a solution of sodium hydroxid; diluted to 500 c.c. with water, instead of 1,000 c.c. (to correspond to the reduction in the amount of the drug used); and the amount of phthalein estimated by comparison with the Dunning colorimeter. Cloudy urine was filtered before making the reading, and if the results were at all doubtful, the diluted urine was mixed with equal parts of water, another reading made and the result of the reading doubled. The Dunning colorimeter was used, partly because a Duboscq colorimeter was not available at the hospital, but chiefly because of its low cost and greater practicability for the use of the general practitioner. The results by this method are admitted to be reasonably accurate.

We regret that so many of the estimations were made only at the end of the

first hour. At the beginning of the study, we had decided to use the one-hour period only. Later, we utilized the two-hour period in the younger infants, catheterizing only once. The earlier results for one hour are included, however, as they may be compared with other results for the same period of time.

The cases are grouped in Table 1 as follows: Group I, Acute Infections; II, Miscellaneous Diseases; III, Acute and Chronic Nephritis; IV, Cardiorenal Disease; V, Pyelitis.

In preparing a summary of the results in the various groups, we found no noteworthy difference in the phthalein elimination of patients with albumin and casts in the urine — apart from the true nephritic groups — and of those whose urinary findings were negative.

While absolute accuracy demands catheterization at the end of both the first and second hour periods, it is admitted that voluntary urination in the nonobstructive types of genito-urinary diseases gives results which are quite accurate. In a comparison of percentages found in our catheterized and uncatheterized patients, the differences were negligible.

Table 2 gives the condensed results for the two-hour periods; Table 3 for one-hour, and Table 4 for total results. In Table 5 all cases are grouped according to their ages, except those with nephritis, and Nos. 1 and 27 (Table 1, Group II).

In the groups of acute infections, miscellaneous diseases and pyelitis (Table 1, Groups I, II and V) no marked diminution in the amount of phthalein eliminated was noted, except in two of the three patients suffering from tuberculous meningitis. One of these (No. 1) died on the same day that the test was made, and the low phthalein elimination (15 per cent. in two hours) was of no clinical significance. The second patient (No. 27) gave less than 5 per cent. of phthalein in two hours, but lived for seven days. The presence of large amounts of albumin and an excessive number of leuckocytes in the urine suggests the possibility of tuberculous lesions in the kidneys, which would account for their poor function. Neither of these cases is included in any of the summaries. The cases of nephritis (Table 1, Groups III and IV) showed a distinct diminution in phthalein percentages, as would be expected. Presumably all of them belonged to the type of parenchymatous nephritis. None died under observation except the patient with cardiorenal disease (No. 57, Group IV), whose death was cardiac and not uremic.

The case of pernicious anemia (No. 38, Table 1, Group II) showed an output of 62.5 per cent. for two hours, although the red cells fell as low as 200,000 in one of the counts made previous to the test. Death did not occur until fifty-seven days after the test.

TABLE 1.—Phenolsulphonephthalein Elimination in Various Groups

GROUP I, ACUTE INFECTIONS

No.	Age	Sex	Diagnosis	Day of Disease	Remarks	Result	Urine, Albumin	Microscopic Examination	Phthalein Test		
									1 Hr.	2 Hr.	Total
2	9 mos.	♂	Acute bronchitis	5	Temperature 98-101	Recovered	2 neg. 2 tr.	4 negative	50	20-25	70-75
21	9 yrs.	♂	Acute bronchitis	5	Afebrile; voided	Recovered	3 neg.	3 negative	50-55	20	70-75
24	10½ mos.	♂	Acute bronchitis	18	Temp. 98.4-100	Recovered	3 neg.	3 negative	60	10-15	70-75
25	13 mos.	♂	Acute bronchitis	6	Temp. 100	Improved	1 neg. 2 tr.	1 hyaline and cylindroids +; 3 leuko. +	50	15	65
30	4 yrs	♂	Acute bronchitis	?	Temp. 98.2-100; voided	Recovered	3 neg.	3 negative except few cal. ox. cryst.	45	20	65
63	5½ yrs.	♂	Acute bronchitis	5	Temp. 98-99.4	Recovered	1 tr.	1 few hyaline	45	—	—
12	6 mos.	♂	Acute bronchitis	14	Afebrile 3 days	Recovered	3 neg.	3 negative	45	15	60
35	6 yrs.	♂	Acute bronchitis	20	Afebrile 7 days	Recovered	3 neg.	3 negative	55	25	80
26	9 mos.	♂	Bronchopneumonia	9	Temp. 99.2	Died 17 days after	2 +	2 cylindroids; leuko. +++	45-50	20	65-70
45	6½ mos.	♂	Bronchopneumonia	15	Afebrile for 3 days	Recovered	2 tr.	2 gran. cast ++	30	25	55
52	5 yrs.	♂	Lobar pneumonia	7?	Afebrile for 4 days; voided	Recovered	2 tr.	2 cylindroids; 1 leuk. ++	35	25	60
39	6 yrs.	♂	Lobar pneumonia	25	Afebrile for 10 days; von Pirquet +; voided	Recovered	1 tr. 1 neg.	1 few hyaline and dark gran. casts; 1 neg.	70	10-15	80-85
20	1 yr.	♂	Acute otitis media	9	Temp. 99.4	Recovered	3 neg.	3 negative	35	5-10	40-45
50	6 mos	♂	Ac. otitis media and retropharyngeal absc.	?	Temp. 100.3	Recovered	2 tr.	2 negative	30	—	—
32	8 yrs	♂	Typhoid fever	21?	Afebrile 2 days; voided	Recovered	2 neg. 1 tr.	3 negative	60	10	70
33	7 yrs.	♂	Typhoid fever	40	Afebrile several days; voided	Recovered	3 neg.	2 negative; 1 few gran. casts	—	70	70
1	4 yrs.	♂	Tb. meningitis	35	Very poor condition	Died in few hours	1 tr.	1 leuko. +++	0	15	15
22	19 mos.	♂	Tb. meningitis	8	Very poor condition	Died 3 days later	1 tr.	1 leuko. ++	60	15	75
27	3½ mos.	♂	Tb. meningitis	?	Very poor condition	Died 7 days later	3 ++	3 leuko. ++++	0	5	5

60	10 mos.	♂	Chronic bronchitis	27	.....	Improved	2 neg. 1 tr.	3 negative	—	75	75
47	4 yrs.	♂	Catarrhal jaundice	12	.....	Recovered	2 neg. 1 tr.	2 negative; 1 leuko. ++	30	20	50
9	18 mos.	♂	Tb. pleurisy	30	von Pirquet +	Improved	1 ft. tr.	1 negative	45	—	—
3	10 mos.	♂	Hydrocephalus	300	von Pirquet +	Unimproved	6 neg.	6 negative	—	65	65
29	17 mos	♂	Infantile atrophy	90	Poor condition	Unimproved	2 neg. 1 tr.	2 neg.; 1 few gran. casts	50	—	—
54	7 mos	♂	Infantile atrophy	180	Poor condition	Improved	3 neg.	2 neg.; 1 few gran. casts	—	80	80
7	7 mos.	♂	Infantile atrophy	33	Poor condition	Improved	3 neg. 1 tr.	4 negative	60	—	—
10	3 mos.	♂	Infantile atrophy	45	Fair condition	Recovered	2 neg.	2 negative	60	10	70
13	2 mos.	♂	Infantile atrophy	?	Fair condition	Recovered	3 neg.	3 negative	40	—	—
15	4 mos.	♂	Infantile atrophy	54	Good condition	Recovered	3 neg.	3 negative	55	—	—
17	3 mos.	♂	Infantile atrophy	90	Poor condition	Recovered	3 neg.	3 negative	65	—	—
18	5 wks.	♂	Infantile atrophy	35	Poor condition; received breast milk	Recovered	4 neg.	4 negative	45	—	—
36	3 mos.	♂	Infantile atrophy	?	Poor condition	Died in 6 days	3 neg.	3 negative	—	70	70
41	4 mos.	♂	Infantile atrophy	120	Poor condition	Unimproved	1 neg.	1 negative	35	5	40
64	8 mos.	♂	Infantile atrophy	60	Fair condition	Recovered	3 neg.	3 negative	45	—	—
67	3 mos.	♂	Infantile atrophy	60	Fair condition	Recovered	3 neg.	3 negative	55	—	—
73	2 mos.	♂	Infantile atrophy	60	Poor condition; fed on breast milk	Recovered	3 neg.	3 negative	35	—	—
72	2 mos.	♂	Infantile atrophy	60	Poor condition	Recovered	2 neg. 1 tr.	2 neg.; 1 few hyaline and gran. casts; leuko. ++	20-25	—	—
44	3 mos.	♂	Infantile atrophy	22	Poor condition	Died 28 days later	3 tr.	2 hyaline and granular casts +; 1 leuko. ++	30	—	—
5	4 mos.	♂	Infantile atrophy	68	Fair condition	Recovered	4 neg.	4 negative	—	60	60
74	7 mos.	♂	Infantile atrophy	Since birth	Poor condition	Improved	1 neg.	1 negative	50	—	—
75	7 mos.	♂	Infantile atrophy	Since birth	Poor condition	Improved	1 neg.	1 negative	60	20	80
40	5½ mos.	♂	Chr. enteritis, gonorrheal epididymo-orchitis	35	Fair condition	Recovered	2 neg. 2 tr.	1 few gran.; 3 negative	50	10-15	60-65
4	5 mos.	♂	Chronic enteritis	40	Good condition	Recovered	4 neg.	4 negative	—	60	60
19	5 mos.	♂	Chronic enteritis	35	Good condition	Recovered	3 neg.	3 negative	—	70	70
61	6½ mos.	♂	Chronic enteritis	30	Fair condition; Temp. 99-100	Recovered	3 neg.	2 neg.; 1 gran. casts +	45	—	—

TABLE 1.—PHENOLSULPHONEPHTHALEIN ELIMINATION IN VARIOUS GROUPS—(*Continued*)

GROUP II—(*Continued*)

No.	Age	Sex	Diagnosis	Day of Disease	Remarks	Result	Urine, Albumin	Microscopic Examination	Phthalein Test		
									1 Hr.	2 Hr.	Total
55	13 mos.	♂	Chronic enteritis	30	Fair condition; Temp. 98–102; von Pirquet +	Improved	2 neg.	2 negative	40	—	—
43	5 mos.	♂	Acute enteritis	7	Poor condition Temp. 98–103	Improved	5 neg. 4 tr.	6 neg.; 2 few hyl. casts; 1 few gran. casts	50	15	65
34	10 mos.	♂	Indigestion	14	Fair condition	Recovered	1 neg. 1 tr.	2 negative	—	80	80
8	3 mos	♂	Indigestion	15	Good condition; von Pirquet ++	Improved	3 neg.	3 negative	50	20	70
11	3 wks.	♂	Indigestion, edema	9	Good condition; fed breast milk	Recovered	3 neg. 1 tr.	4 negative	—	60	60
14	4½ mos.	♂	Indigestion	49	Very good condition	Recovered	3 neg.	3 negative	55	—	—
23	6 yrs.	♂	Indigestion	?	Poor condition; von Pirquet + voided	Improved	3 neg. 4 tr	7 negative	25	35	60
46	3½ mos.	♂	Indigestion	40	Good condition	Recovered	3 neg.	3 negative	60	—	—
53	10 mos.	♂	Indigestion	29	Good condition	Recovered	2 neg.	2 negative	35	—	—
70	3 mos.	♂	Indigestion	18	Good condition	Recovered	3 neg.	3 negative	60	—	—
28	5 mos.	♂	Indigestion	16	Fair condition	Recovered	2 neg.	2 negative	45-50	25	70-75
31	2 yrs	♂	Indigestion	12	Fair condition	Recovered	7 neg.	7 negative	—	80	80
71	3 mos.	♂	Indigestion	40	Fair condition	Recovered	3 neg.	3 negative	60-65	15	75-80
61	14 mos.	♂	Congenital lues	Since birth	Fair condition; 2 Wass. +	Improved	5 tr.	2 negative; 3 leuko. ++	65	—	—
66	7 mos.	♂	Hydrocephalus	Since birth	.....	Unimproved	4 neg.	4 negative	35	—	—
38	3 yrs.	♂	Pernicious anemia	70	Voided; poor condition; Temp. 98-101	Died 57 days later	9 neg. 1 tr.	9 neg.; 1 few gran. casts	45	15-20	60-65
56	4½ yrs.	♂	Intestinal parasites	?	Good condition Temp. 99–100	Recovered	6 neg. 2 tr.	8 negative	35	30	65

GROUP III, NEPHRITIS

No.	Age	Sex	Diagnosis	Day of Disease	Remarks	Average Daily Amount Urine, Ounces	Urine,	Microscopic Examination	Phthalein Test		
									1 Hr.	2 Hr.	Total
6	7 yrs.	♂	Chronic nephritis	?	Syst. B. P. 120; diast. 68; no edema; seen 3 mos. later; still had alb. and casts	38	13 +	13 few hyl. and lt. gran. casts	50	15	65
42	10 yrs.	♂	Chronic nephritis 1 yr. after scarlatina	365	Syst. 112–108; diast. 90-82; no edema; had alb. and casts before adm.; voided	38 (19–43)	6 neg.	5 neg.; 1 few hyl. and dark gran. casts	30-35	15	45-50
62	9 yrs.	♀	Chronic nephritis; sinus arrhythmia	64	Syst. 136; diast. 88; slight edema, legs and eyelids; Temp. 99–100; voided	22	3 neg. 3 +	5 hyl., gran., waxy and epithelial casts +; 1 neg.	40	10-15	50-55
68	4 yrs.	♀	Acute nephritis	21	Syst. 110; diast. 70; marked edema; Temp. 99-100	6½ to 10½	18 +	18 hyl., gran. and blood casts +	3/7/17 — 3/19/17 10	3/7/17 30-35 3/19/17 15	30-35 25
65	3 yrs.	♂	Acute nephritis	15	No edema; Temp. 99.8–100	28	10 ++ to +++	10 gran. casts ++; blood casts +; leuko. +++	35	5	40
51	9 yrs.	♀	Acute nephritis	38	Syst. 210; diast. 187(?); slight edema eyelids; died 7 days later; voided	24	15 ++ to +++	15 hyl. and gran. casts +; leuko. +++	20	15	35
37	5 yrs	♂	Acute nephritis	16	Syst. 82–92; diast. 60–64; no edema; toxic; had suprsn. urine at first; recovered; voided	20 to 22	8 tr.	8 hyl. and gran. casts +	11/11/16 25 11/14/16 50	11/11/16 20 11/14/16 15-20	45 65-70
48	7 yrs.	♂	Acute nephritis	38	Syst. 105; diast. 55; moderate edema legs Temp. 98–100	36	11 tr.	11 hyl. and gran. casts +	40	10	50

GROUP IV, CARDIORENAL

57	6½ yrs	♀	Chronic endocarditis; chronic nephritis	365	Syst. 130; diast. 80; marked edema; Temp. 97–102; salt-free diet; voided; died 6 weeks later	22	10 +++	10 hyl. and gran. casts ++	15	25	40

TABLE 1.—PHENOLSULPHONEPHTHALEIN ELIMINATION IN VARIOUS GROUPS—(*Continued*)

GROUP V, PYELITIS

No.	Age	Sex	Diagnosis	Day of Disease	Remarks	Result	Urine, Albumin	Microscopic Examination	Phthalein Test		
									1 Hr.	2 Hr.	Total
16	6 mos.	♂	Pyelitis	27	No alb. or casts for 2 wks. before test	Recovered	3 neg. 10 tr.	Pus cells, 15-20 to high power field uncentrifuged urine; hyl. casts occas.	30	15-20	45-50
49	4 yrs	♀	Pyelitis	42	.....	Improved	39 ++ to +++	Pus cells ++ to +++; 4 few hyl. casts; 1 few gran. casts	40	25	65
58	9 mos.	♂	Pyelitis	40	.....	Recovered	2 neg. 14 tr.	Pus cells ++ to +++	45	—	—
69	11 mos.	♂	Pyelitis	?	Temp. 100-103	Recovered	13 tr.	Pus cells 3 to 28 to high power field uncentrifuged	60	—	—

TABLE 2.—CONDENSED RESULTS FOR TWO-HOUR PERIODS

Groups	Number of Cases	Average Percentage of Phthalein Eliminated			Extremes		
		1 Hr.	2 Hrs.	Total	1 Hr.	2 Hrs.	Total
I and V	16	47.8	18	65.8	30-70	7.5-25	42.5-82.5
II	12	45.8	18.8	64.6	25-62.5	5 -30	40 -80
III and IV	9	31.75	15	46.75	10-50	5 -25	25 -67.5

Table 2 emphasizes the fact that there was no noteworthy difference between the results obtained in the acute infections and in the miscellaneous diseases. There is, therefore, no further object in separating them. In general, the proportion of phthalein eliminated in the first and second hours corresponds to that found in adults; nor was there any ascertainable reason for the occasional discrepancies of a large output in the second hour, such as was found in Cases 45 and 52, although in Case 57 the marked edema may have been the cause of delayed elimination. As the maintenance of the normal proportion in the first hour is not essential, while the total result for two hours is generally accepted for a standard interpretation, we would advocate the estimation of only the total amount of phthalein eliminated in two hours in children who require catheterization, thereby avoiding the necessity for repeating it.

TABLE 3.—RESULTS FOR ONE-HOUR PERIODS

Groups	Number of Cases	Average Percentage of Phthalein Eliminated in the First Hour	Extremes
I, II and V	53	46.9	22.5-70

This table includes a number of patient on whom only a 1-hour observation was made. The results very closely approximate those in Table 2.

TABLE 4.—TOTAL RESULTS

Groups	Number of Cases	Average Percentage of Phthalein Eliminated in Two Hours	Extremes
I, II and V	39	66	40-82.5

This table includes the patients on whom only one observation was made at the end of two hours. Again, the results closely approximate those in Table 2.

TABLE 5.—Grouped According to Ages, Etc.

GROUPS I, II AND V

Age	Period	No. Cases	Per Cent.	Per Cent.
Under 3 months	1-hour	11	47.7	(22.5-65.0)
	2-hour	5	69.4	(60.0-77.5)
3 to 6 months	1-hour	11	44.3	(30.0-60.0)
	2-hour	11	61.4	(40.0-80.0)
6 to 12 months	1-hour	13	48.6	(35.0-60.0)
	2-hour	8	69.4	(42.5-80.0)
1 to 2 years	1-hour	6	51.6	(40.0-65.0)
	2-hour	3	73.0	(65.0-80.0)
Over 2 years	1-hour	12	44.8	(25.0-75.0)
	2-hour	12	66.9	(50:0-82.5)

From a study of Table 5 it is clear that the ages of the patients had no influence on the elimination of phthalein. Even Patients 11 and 18 (Table 1) aged 3 and 5 weeks, showed an output of 60 per cent. for two hours and 45 per cent. for one hour, respectively.

CONCLUSIONS

1. The observation is confirmed that the elimination of phenolsulphonephthalein is not markedly decreased in any disease other than renal.

2. Even the youngest infants and children show about the same capacity for phthalein elimination as do adults.

3. Preliminary catheterization in the absence of retention of urine is unnecessary.

4. For purposes of comparison, a uniform technic should be adopted and maintained.

5. We believe that in children a single collection exactly two hours after the injection into the lumbar muscles of 6 mg. of phthalein, should be the method of choice. The necessity for continuous or repeated catheterization thereby would be avoided.

6. An entirely different standard must be used for the accelerated output resulting from intravenous injections. The latter need only be employed when local conditions, such as marked edema, prevent the use of the intramuscular route.

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THE USE OF PANCREATIC VITAMIN IN CASES OF MARASMUS *

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INTRODUCTORY

Vitamin was first isolated from rice polishings in 1911 by Casimir Funk and shown by him to be the agent which prevented beriberi. It was also in this year that Mendel and Osborne did their comprehensive work on the feeding of single purified proteins to white rats. In the latter work it was established that in addition to nutrients the diet of a growing rat demanded the presence of certain substances hitherto unknown, and which these workers found present in protein-free milk and in centrifuged butter fat. Funk had meanwhile not only extended his isolation of vitamin to other substances than rice polishings — among them yeast — but had shown that aside from the effect on polyneuritic conditions the vitamin was an essential factor in growth stimulation. From these beginnings the development of the importance of vitamin as a growth factor has been rapid. Of all the studies, those of E. V. McCollum of Wisconsin, and his co-workers, perhaps deserve most attention. McCollum has summed up the dietary factor as follows: In addition to a suitable nutrient content, a growing animal demands in his diet:

1. The presence of a "fat-soluble A" (his name for Mendel's butter fat factor).

2. The presence of a "water-soluble B" (his name for Funk's vitamin).

3. The absence of any toxic factors.

Experiments have shown that whatever the composition of vitamin, it is probably not a simple amin. The nomenclature problem would be easier to settle if the substance had been satisfactorily identified chemically. Unfortunately, all attempts to purify it or to isolate it in an approximately pure form have resulted in failure and in loss of power on the part of the vitamin-containing factor. This result has given rise to certain controversies and hypotheses that tend to confuse the general student of the subject. Funk, for example, claims that Mendel's butter fat does not contain a new type of vitamin, but is merely contaminated with the water-soluble vitamin he has described.

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* From the Department of Pathology of the New York Hospital.

McCollum, on the contrary, is thoroughly convinced that there are at least two types of growth-producing substances, and has suggested dropping the name vitamin altogether and substituting the names given above as temporary descriptive terms pending the settlement of the problem of chemical structure. Hess has shown that however much scurvy may resemble beriberi, the yeast vitamin that curbs the latter does not control the former disease, and furthermore, that the orange juice that cures scurvy is not a growth stimulant, and in that sense at least is not a vitamin.

Still another difficulty in the study of vitamins lies in the lack of any chemical test for their presence. At present, we have only two ways of determining this, namely, by producing polyneuritic conditions in pigeons through the feeding of polished rice and then treating the birds with the vitamin-containing substance, or by feeding rats on a maintenance diet and then by the addition of the vitamin to the diet noting the upward tendency of the growth curve as a result. These tests require careful control and involve many factors. Even now we do not know whether the antineuritic vitamin is identical with the growth-producing vitamin, whether there is a group of chemical substances with similar properties, or particular substances with specific function. If the latter is true, then orange juice contains a vitamin that is specific for scurvy. If, on the other hand, vitamins are substances which combine the power of growth stimulation with antineuritic properties, then orange juice contains no true vitamin at all.

In spite of all this confusion incident to the status of the problem today, the study is making progress. A marked addition to the practical possibilities of the subject was developed when Seidell established the feasibility of obtaining active vitamin from its crude solution by means of a special form of fuller's earth. This form, known as Lloyd's reagent, has the power, when shaken with a crude vitamin extract, of adsorbing the vitamin. Apparently, no loss of activity occurs in the vitamin in the process, no appreciable amount of contaminative substance is removed from the solution by the reagent, and the result is the possibility of an activated agent whose bulk is composed of an inert, harmless-to-man material, and which has the properties of a pure (?) vitamin as far as effects go.

PANCREATIC VITAMIN

In a previous communication, Eddy has confirmed the efficiency of this means of separation for the removal of pancreatic vitamin from its aqueous solution. In the feeding experiment about to be described the Lloyd powder, activated by an aqueous solution of pancreatic vitamin, was used. The steps in the preparation may be briefly summarized as follows:

Pancreatic glands of lambs were obtained within twenty-four hours of their removal and minced in a meat chopper. These minced glands were thoroughly extracted with 95 per cent. alcohol to which had been added enough hydrochloric acid to make it approximately 0.8 per cent. acid. The acid-alcohol extract was filtered and the filtrate evaporated to dryness before the fan at 25 C. The residue was thoroughly extracted with water and the water extract filtered and concentrated before the electric fan to such a volume as to make 1 c.c. correspond to 2.7 gm. of pancreas. This was an arbitrary unit selected as a means of standardizing subsequent preparations. One c.c. of this extract contained 0.0075 gm. of nitrogen. To a liter of this water extract was then added 50 gm. of Lloyd's reagent and the mixture made thorough by shaking in a mechanical shaker for thirty minutes. This mixture was left to stand over night and at the end of that time the sediment was filtered off with a suction funnel, dried before the fan, repowdered in a mortar, and finally dried to constant weight in a vacuum desiccator over sulphuric acid. This dried powder was found by experiments on rats to have the vitamin effect, and the tests with the filtrate indicated that the removal of the vitamin was quantitative. Furthermore, no amino-acids were separated from the solution by the powder. While the amount of nitrogen in the powder varies somewhat with the preparation, it is usually about 0.03 + gm. nitrogen per gram of powder.

The advantages of this powder for dosage are obvious. In the first place, the powder itself is entirely harmless to the animal, being inert except for its adsorbing power. Second, it enables one to give a relatively heavy dose of vitamin without using a large bulk, as 1 gm. of the powder contains the vitamin of 54 gm. of pancreas. Third, the vitamin effect is not modified by the presence of other factors.

Having demonstrated the efficiency of this vitamin preparation in growth stimulation with white rats, it seemed desirable to try its effect in cases of infant malnutrition and especially in cases of marasmus. Up to the present, ten cases have been studied, of which six were cases of marasmus. Nine of these patients were treated in the wards of the New York Hospital. One was treated under our direction at the Babies' Hospital, the case being supplied through the kindness of Dr. F. H. Bartlett.

While the number of cases at present reported is small, the results are suggestive, and are reported here more for stimulation of collateral investigation than because of the conclusiveness of the evidence. As presented, the cases are classified in three groups. Each group will be discussed in detail, and it will suffice here to indicate merely the basis of classification.

Group I: In this group is covered the case of a single patient, John G., a typical marasmic, whose growth stimulation was apparently induced by vitamin while being fed a carefully controlled, practically vitamin-free diet of cereal, orange juice and condensed milk. This case was further controlled by a study of five rats fed on a diet identical with that of the baby and with the vitamin content varied to meet experimental needs.

Group II: In this group are placed five patients, including three

with marasmus, who at the time of beginning the vitamin treatment were declining in weight and whose weight curves were deflected upward without other apparent means than by the addition of vitamin.

Group III: In this group are placed four patients who had begun to gain on the diet supplied, and to whose diet the vitamin was added in the hope of stimulating better growth. These cases add little definite evidence as to the stimulation by vitamin. They show that the addition of the vitamin was followed by growth, but whether this was due to the vitamin or not cannot be demonstrated by the evidence. In some cases the rate of growth was apparently increased.

EXPERIMENTAL

Group I: Patient John G.

The patient was 6 months old on admission to the hospital; weight on admission, 7 pounds 9 ounces; a typical marasmic in appearance.

History.—The chief complaint was continued loss of weight, and the admission diagnosis was malnutrition. Father and mother well; one other child, 2 years old; one miscarriage. This baby was a full term normal child, of normal birth; weight at birth was said to have been 12 pounds; nursed one month; then fed two-thirds water, one-third grade "A" milk; 8 ounces every two hours, and one feeding at night. After a few weeks the infant began vomiting and had green stools, no mucus or curds; five or six movements per day. The baby was sent to a hospital and after three weeks was sent to the country, from which it returned apparently healthy. Then it began to lose weight again, and was being fed at this time 30 ounces boiled water, 3 ounces barley water, 20 ounces grade "A" milk, with two lumps of sugar; 5 ounces every three hours; often the infant refused part of a feeding.

Physical Examination.—Emaciated, facies of an old person; bones prominent; no craniotabes; eyes and ears normal; no rigidity of neck; no pulsations; chest long and slender; ribs prominent; lungs and heart-beat normal.

DISCUSSION

On admission to the hospital, Oct. 9, 1916, the patient was given an observation period of twenty-two days, during which several varieties of diet were tried. During this time the patient's weight varied greatly, as shown by Chart 1, and the net change was a loss of 2 ounces. October 31, the patient weighed 7 pounds 8 ounces, and during the six days preceding this date had declined in weight some 12 ounces (see chart). During the first eighty days the character of the diet was a combination of condensed milk in various strengths, with cereals and a daily allotment of orange juice. To this diet was added at two different periods a dosage of pancreatic vitamin. The dose consisted of 2 gm. of Lloyd's reagent activated by vitamin, 1 gm. being given with a feeding of cereal twice a day. Analysis showed that 1 gm. of this activated vitamin powder contains 0.03 gm. of nitrogen. There is also reason to believe that this indicates a dosage

of not more than 0.12 gm. of vitamin per day. In the accompanying chart (Chart 1) have been indicated the patient's weight curve, the calorie value of the food actually consumed per day, the vitamin periods and various incidents bearing on the progress, such as abscesses, coughs, etc., together with a record of the number of daily stools. Beginning about the seventieth day the patient was gradually transferred from the condensed milk to a whole milk formula. The results of the treatment can therefore be best studied from the chart.

It will suffice, then, to call attention to certain features bearing on the results. For example, it will be noted that from the twenty-first to the twenty-ninth day the addition of the vitamin was accompanied by a marked rise in weight of 8 ounces, though the food consumption was the lowest in the feeding period. On the twenty-ninth day the feedings were increased to gratify the appetite, coincident with the rise in the weight curve, and the net gain in this first vitamin period was 21 ounces in twenty-one days. On the forty-third day the vitamin was discontinued. This change was made to determine whether the growth would continue after the vitamin had been removed from the diet. As has been previously found to hold with rats, the effects of the ingested vitamin apparently continued five days, the patient gaining 6 ounces during this period. During the next four days there was no gain, though the food intake remained the same, 563 calories. Since that number of calories was sufficient to provide growth for a 9-pound boy, and since it bore out the other result, the observations on rats, it seemed to indicate the stimulating power of the vitamin and the failure of growth when vitamin was removed from a diet poor in natural vitamin. At this time the patient was markedly improved in appearance, face oval from tissue formation instead of pinched and wan, bones of the legs well covered and every indication of normal tissue growth. Without changing the diet otherwise, vitamin feedings were resumed on the fifty-third day. The second administration period was for twenty-three days, with a net gain in weight of 8 ounces. At the end of this period the vitamin treatment was stopped and the patient gradually introduced to a whole milk diet. The results indicated that the power to utilize vitamins in such a diet had been acquired and the child has since gone on to complete recovery. He was discharged from the hospital on the one hundred and thirty-eighth day after admission, and at that time weighed 13 pounds, a net gain of 5 pounds 6 ounces since admission.

CONTROL EXPERIMENTS WITH RATS

Five rats were selected and a daily diet of cereal and condensed milk was fed them. Each rat received and completely consumed each day 2 ounces of condensed milk. They received each day as much

cereal of the kind given John G. as they would eat, and the amount consumed was noted by weighing back each day. None of the rats received orange juice. In this respect only did they differ from John G. in the character of their diet. Three of the rats were fed this diet alone and weighed each day. As a result, two of the rats developed

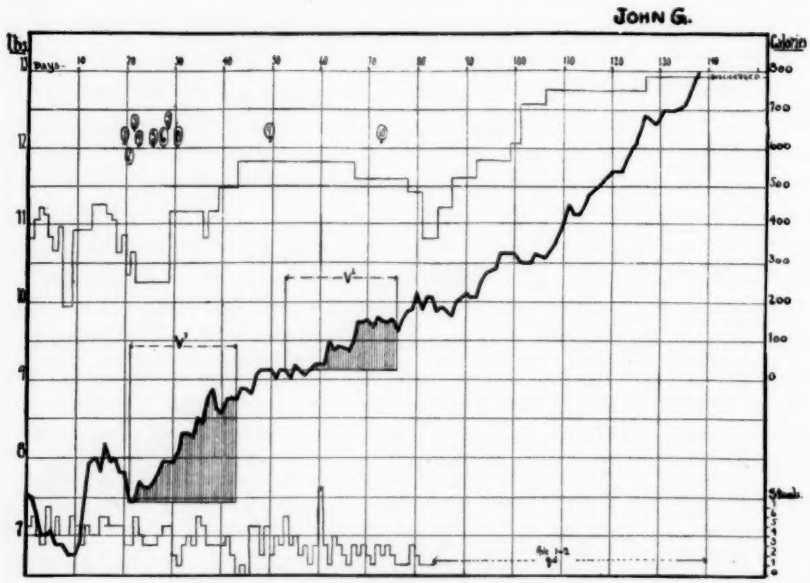

Chart 1.—Group I, No. 1.

Chart 1.—1. On the twentieth day the patient developed a cough. 2. On the twenty-first day the cereal was reduced from three times a day to twice a day. The patient cried during the night. 3. On the twenty-second day the stools showed free starch. 4. On the twenty-third day an anal abscess was opened. The stools continued to show free starch until the twenty-fifth day. 5. On the twenty-fifth day the stools showed soluble starch but no free starch. 6. On the twenty-seventh day the appetite was good and there was no starch. 7. From the twenty-eighth to the forty-third day no starch was observed in the stools. 8. On the thirty-first day the patient developed a cough. 9. From the forty-ninth day to the time of discharge three tablespoonsful of orange juice were given daily. 10. On the seventy-third day the patient developed a bronchitis and mustard paste was applied every four hours up to the eighty-fourth day.

V^1 = From the twenty-first day to the forty-third day the patient received each day 2 gm. of Lloyd powder, activated with pancreatic vitamin. The powder was administered by mixing 1 gm. with each cereal feeding. The result was 20 ounces gain in twenty-two days, a normal growth.

V^2 = After a period of ten days without vitamin, during which the patient settled down to a level growth curve, the treatment described under V^1 was resumed. This was continued from the fifty-third to the seventy-sixth day. The result was the resumption of growth but at a slower rate; 8 ounces were gained in twenty-three days. During the latter part of the period the patient developed a bronchitis. At the end of this period the patient was placed on a whole milk formula. From that time to the time of discharge the patient grew normally.

scurvy and died at the end of twenty-three and twenty-four days, respectively. The remaining one of these three did not develop scurvy. Two of the five rats were given the above diet plus 1 gm. of the activated Lloyd powder (mixed with the cereal) each day. These rats developed no signs of scurvy, but as this was also true of one of the other group, we cannot be sure that this vitamin is antiscorbutic. Experiments are under way to determine this point. The effect of the introduction and removal of vitamin from the diets of these five control rats is shown in Chart 2. The figures are as shown in Table 1.

TABLE 1.—EFFECT OF VITAMIN ON RATS FED JOHN G.'S DIET

	Two Rats Fed on Condensed Milk, Cereal and 1 Gm. Vitamin Powder per Day		Three Rats Fed on Condensed Milk, Cereal and No Vitamin		
	Rat 20	Rat 22	Rat 16	Rat 17	Rat 18
Weight November 8, gm.	68	48	78	66	76
Weight at end of period, gm.	88	73	62 (dead)	67 (dead)	76 (alive)
Days elapsed	13	13	24	23	24
Net gain or loss, gm.	+20	+25	−16	+1	±0
Total cereal eaten, gm.	446	452	768	695	825
Average daily consumption, gm.	34	35	32	30	34

Average daily condensed milk was 2 ounces per day per rat.

The results in this table show clearly two things, namely, that the cereal and condensed milk diet is markedly lacking in natural vitamins, and that the addition of pancreatic vitamin to such a diet is sufficient to convert it into an efficient growth-producing diet. In order to check this matter further, Rats 20 and 22 were deprived of the vitamin for the next twelve days. As in the case of the child, the stimulation of the ingested vitamin apparently continues for some time after stopping its feeding. The results are shown on the chart and in Table 2.

TABLE 2.—EFFECT OF STOPPING THE VITAMIN IN RATS 20 AND 21

	Rat 20	Rat 22
Weight November 21, gm.	88	73
Weight December 3, gm.	88	86
Net gain or loss, gm.	±0	+13
Days elapsed	12	12

During this period the rats were fed on cereal and condensed milk but without any vitamin.

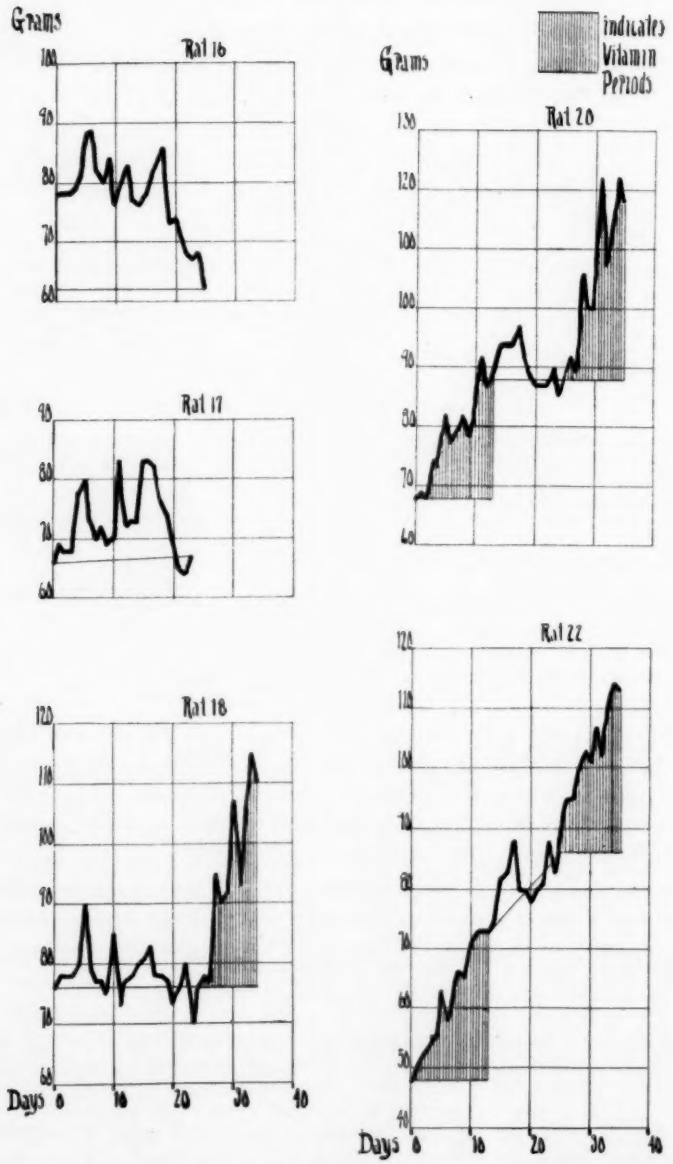

Chart 2.—Group I, No. 2. Rats fed on John G.'s diet with and without vitamin.

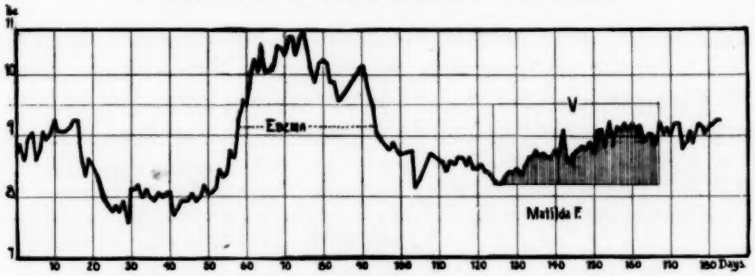

Chart 3.—Group II, No. 1.

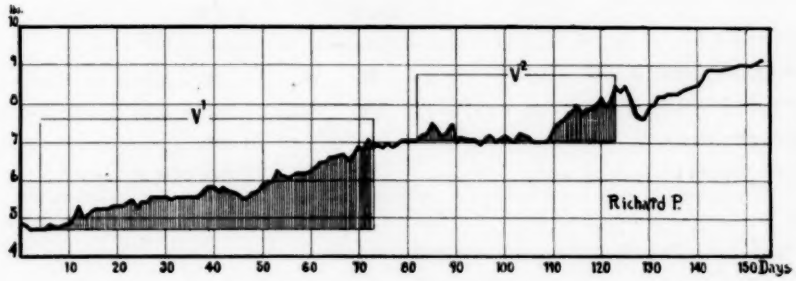

Chart 4.—Group II, No. 2.

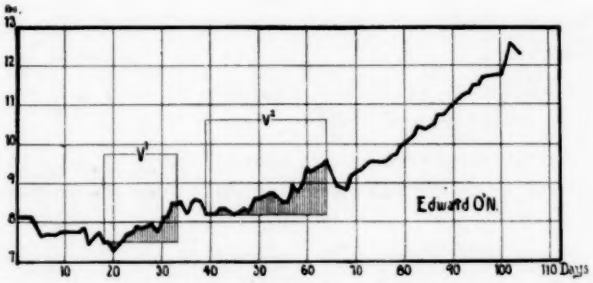

Chart 5.—Group II, No. 3.

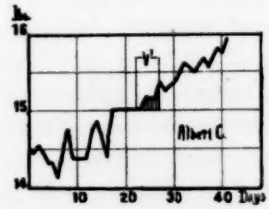

Chart 6.—Group II, No. 4.

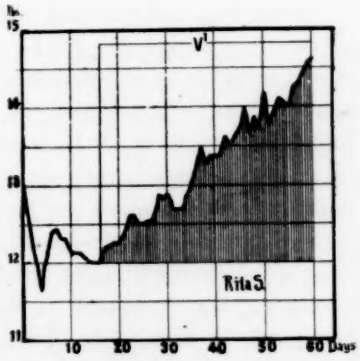

Chart 7.—Group II, No. 5.

Still further to determine the effect of the vitamin on this diet, Rats 20, 22 and 18 were then fed as before, but with the vitamin added for a period of ten days. The marked rise in this period seemed to justify the conclusions reached from the preceding data (Chart 2).

TABLE 3.—Effect of Resuming Vitamin After a Period Without It

	Rats 20, 22, and 18 Were Fed for a Period of Ten Days on Cereal and Condensed Milk, the Addition of 1 gm. of Vitamin Powder per Day Following a Nonvitamin Period		
	Rat 20	Rat 22	Rat 18
Weight December 3, gm.	88	86	76
Weight December 14, gm.	118	113	111
Net gain, gm.	+30	+27	+35
Days elapsed	10	10	10

CONCLUSIONS

From the combined results with the patient and the rats the evidence seems to warrant the following conclusions:

1. A diet of condensed milk and cereal is markedly deficient in natural vitamins.

2. The addition of pancreatic vitamins to such a diet influences the growth of both rats and child.

3. The dosage employed in the case of John G. was sufficient to produce growth of a normal rate, though not to the extent noted in the rats.

4. The treatment produced no harmful effects of any sort.

Group II: Patients: Matilda F., Richard P., Edward O'N., Albert C. and Rita S.

These five children had suffered loss of weight or failure to grow on the diets supplied. These diets presented considerable variety, but all the patients were either declining in weight or static at the time the vitamin was administered, and in all cases this administration was followed by growth without other change in the diet. The diet in no case was increased until growth had begun, and demands for more food became necessary on this account.

Two of these children were too small to take cereal when the treatment was begun (Richard and Edward). These infants received their first dosage in the form of the aqueous extract, 10 c.c. being added to a bottle of milk, twice a day. When these children became able to eat cereal they received the activated powder also. To the other three

the vitamin was given as in the case of John G. — 1 gm. activated powder mixed with a feeding of cereal twice a day.

In the case of Matilda F. (Babies' Hospital case) the child received her first impulse toward normal growth after 123 days of experimentation with other diets. The five charts of Group II (Charts 3, 4, 5, 6 and 7) show the results of the treatment graphically; the figured weight gains are shown in Table 4.

TABLE 4.—(CHARTS 3 TO 7) WEIGHT GAINS IN GROUP II

	Matilda F.	Richard P.	Edward O'N.	Albert C.	Rita
Ounces gained or lost in previtamin period	—9	—2	—10	+8	—16
Number days elapsed	124	4	18	22	16
Rate of gain or loss	—0.07*	—0.5*	—0.55*	+0.36*	—1
Ounces gained in first vitamin period	+16	+30	+15	+6	+42
Number days elapsed	43	69	15	6	44
Rate of gain	+0.37*	+0.43*	+1.0*	+1.0*	+0.95*
Ounces gained or lost in first postvitamin period	+1	+4	—4	+9	
Number days elapsed	16	9	6	14	
Rate of gain or loss	+0.06*	+0.44*	—0.66*	+0.64*	
Ounces gained in second vitamin period	....	+24	+23		
Number days elapsed	....	41	25		
Rate of gain	....	+0.58*	+0.92*		
Ounces gained in second postvitamin period	....	+10	+42		
Number days elapsed	....	31	40		
Rate of gain	....	+0.32*	+1.05*		

* Rate determined by dividing total gain or loss in ounces by number of days elapsed.

All of these patients have now fully recovered, and sufficient time has elapsed to indicate permanent recovery.

These cases seemed to offer further evidence for the conclusion that pancreatic vitamin in the dosage and form given offers a medium through which growth may be stimulated in this type of patient. In the cases of Edward and Richard the evidence was especially strong. In both a cessation of the vitamin resulted in a lowered rate, and the restoration to a higher rate was obtained by resuming the vitamin without other change in the diet. These two cases also demonstrate another feature of the treatment, namely, that the use of vitamin ultimately results in the development of the power to use the natural vitamins in the food, for when these babies were put on a whole milk diet after a second period of vitamin they were able to grow on it.

At the beginning of the experiment they could not utilize such a diet for growth. By stopping the vitamin treatment and noting whether this power has developed, one has a check on the duration of the treatment.

In all these five cases the babies gave every indication of marked improvement physically. They were all discharged as cured and sufficient time has elapsed to feel certain of the permanence of the recovery.

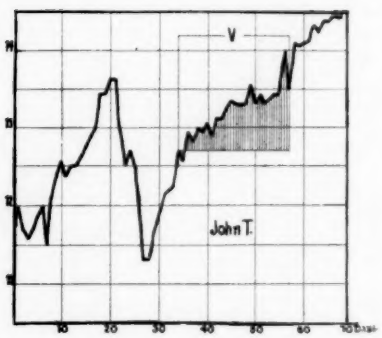

Chart 8.—Group III, No. 1.

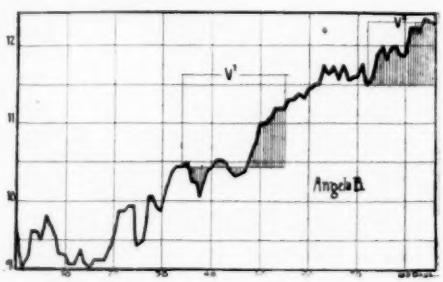

Chart 9.—Group III, No. 2.

GROUP III: Patients: Arthur J., Elizabeth C., Angela B. and John T.

These four children had suffered from malnutrition and had been tried on various diets. At the time the vitamin was begun they had already started to grow on a diet consisting of a whole milk formula

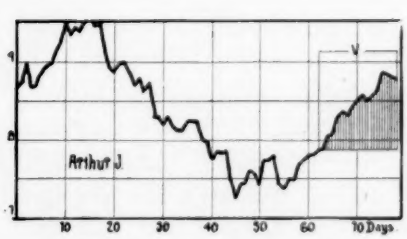

Chart 10.—Group III, No. 3.

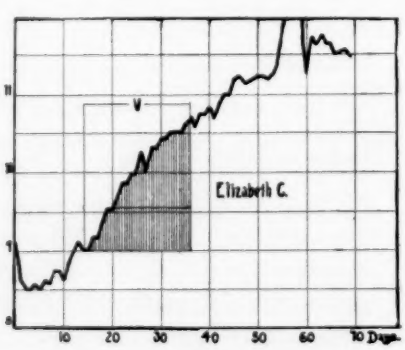

Chart 11.—Group III, No. 4.

and cereal. Vitamin was added to this diet to see if it would increase the effect of the natural vitamin in the milk. The graphs are shown in the four charts of Group III (Charts 8, 9, 10 and 11). The figures showing the gain or loss will be found in Table 5.

TABLE 5.—(CHARTS 8 TO 11) SHOWING GAIN OR LOSS IN GROUP III

	John T.	Angela B.	Arthur J.	Elizabeth C.
Ounces gained or lost in previtamin period	+15	+23	—13	—2
Number days elapsed	34	34	62	14
Rate of gain or loss	+0.44*	+0.68*	—0.2*	—0.14*
Ounces gained in first vitamin period	+13	+12	+15	+27
Number days elapsed	23	21	17	22
Rate of gain or loss	+0.56*	+0.54*	+0.88*	+1.22*
Ounces gained or lost in post-vitamin period	+17	+5	....	+13
Number days elapsed	12	17	....	33
Rate of gain	+1.41*	+0.29*	....	+0.39*
Ounces gained in second vitamin period	....	+12		
Number days elapsed	....	14		
Rate of gain	....	+0.85*		

The cases in Group III are not offered as positive evidence. At best they seem to indicate that the addition of vitamin to the diet may have increased the growth rate in certain of the cases, but from the fact that growth had already begun, this effect cannot be demonstrated to be due to the vitamin. They are included in order to present a complete picture of the entire experiment. At least they do not contradict the evidence of Groups I and II.

SUMMARY

The use of pancreatic vitamin seems to promise definite hope of success as an agent for stimulating the growth of marasmic children. Hess has shown a similar effect of yeast vitamin, but our results do not permit, as yet, of conclusions as to the relative merits of the two sources of vitamins.

The dosage is not yet satisfactorily worked out and the conditions under which the effect is produced are not yet defined. These various features are under investigation and the results presented above are given as a stimulus to further work, rather than as conclusive evidence.

VARIATIONS IN INFANTS OF TOTAL BLOOD SOLIDS AND THE CONCENTRATION OF SODIUM CHLORID IN THE PLASMA*

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NEW YORK

In the course of some investigations at the Babies' Hospital on nutritional edema of infants, determinations of total solids of the blood and chlorid content of the plasma were made on a large number of children. Some interesting facts which were brought out in the course of this work are here presented. A discussion of the significance of the findings will not be attempted. Therefore, a review of the extensive literature on the osmotic pressure of the blood and the relation of blood water and salts to the fluids in the tissues, conditions which have been supposed to have some importance in the production of this form of edema, is hardly called for here.

The literature of the two subjects which are considered in this communication is very limited. We have been unable to find reported any results of chlorid determinations in the plasma of infants' blood. Also, very few figures are obtainable on total solids of the blood, although the subject has been discussed by many pediatrists. Lederer[1] determined the blood water of suckling dogs. Lust[2] has reported a number of observations on blood water of normal infants. His results will be referred to later. Gettler and Baker,[3] at Bellevue Hospital, have carried out a very complete investigation of the blood of normal adults. The results given for total solids and chlorid in the plasma of adults are of especial interest for comparison with the figures obtained by us for normal infants.

In all, seventy-nine determinations of blood solids and eighty-one of blood chlorid were made on sixty-seven different children. The ages ranged from 5 weeks to 6 years, but most of the subjects were under 2 years. Thirteen were well-nourished normal children from 2 months to 6 years of age; some of them were breast fed, some were fed with modifications of cow's milk and some were on a mixed diet. The remainder were suffering from quite a wide variety of diseases, the principal groups being lobar pneumonia, bronchopneumonia, tetany,

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* From the Laboratories of the Rockefeller Institute for Medical Research and the Babies' Hospital.

1. Lederer: Ztschr. f. Kinderh., 1914, **10,** 367.
2. Lust: Jahrb. f. Kinderh., 1911, **73,** 85 and 179.
3. Gettler and Baker: Jour. Biol. Chem., 1916, **25,** 211.

marasmus and intestinal disturbance, nutritional edema, sclerema, and one case of poliomyelitis. Three of the children had highly concentrated blood. The ages of the abnormal children corresponded closely with those of the normal children. The diet was various with these also.

Technic Employed.—About 5 c.c. of blood were drawn into a syringe. One portion was transferred to a platinum dish and the remainder to a tube containing about a gram of powdered potassium citrate. The portion in the platinum dish was used to determine the total solids. This was immediately weighed, evaporated on the waterbath, and dried to constant weight in an oven at about 100 C. Total solids are reported as per cent. by weight. The citrated blood was centrifugalized to separate the plasma from the cells. The protein was then removed from the plasma according to the method of McLean and Van Slyke for the determination of blood chlorid.[4] In the beginning their method was used for the determination of the chlorid in the filtrate. As identical results were obtained by the simpler Volhard method, however, most of the determinations of chlorid, after the preliminary removal of the protein, were made by the Volhard method. The figures are reported as grams of sodium chlorid in 1 c.c. plasma.

Normal Infants.—The results obtained with normal infants are shown in Table 1. Comparing the averages here with those of Gettler

TABLE 1.—NORMAL CHILDREN

Name	Date	Age, Months	Water in Blood, Per Cent. by Weight	Total Solids, Per Cent. by Weight	Chlorid in 1 C.c. Plasma Computed as Gm. of NaCl
Tessie R.	Oct. 6	54	82.39	17.61	0.00577
Julius H.	Oct. 10	48	82.43	17.57	0.00592
Helen H.	Oct. 10	72	81.83	18.17	0.00563
Lawrence S.	Oct. 23	20	82.23	17.77	.....
Emmanuel D.	Oct. 23	14	82.35	17.65	.....
John D.	Oct. 23	2	.....	.....	0.00626
Ralph S.	Oct. 23	5	83.69	16.31	0.00574
Ernest A.	Oct. 24	6	82.95	17.05	0.00641
Paul S.	Oct. 24	17	83.77	16.23	0.00577
Dorothy C.	Oct. 26	7	82.19	17.81	0.00595
Frank M.	Oct. 31	8	81.73	18.27	0.00600
Henry R.	Nov. 4	14	82.41	17.59	0.00536
John M.	Nov. 8	17	83.30	16.70	0.00577
Average			82.61	17.39	0.00587

and Baker for adults (Table 9), it is seen that the values for chlorid are almost identical, while those for blood solids show quite a marked difference, the range in infants being from 16 to 18, in adults from 20 to 25 per cent. of the total blood. Lust reports an average of 18 per cent. blood solids for normal infants, which agrees fairly well with our own findings. The range of values found for normal infants is narrower than that reported for adults, in respect both to blood solids and chlorid. A study of these findings does not reveal any correspondence between the variations in blood solid content and those in sodium chlorid in the plasma. The extreme values in each correspond to average values in the other.

4. McLean and Van Slyke: Jour. Biol. Chem., 1915, **21**, 361.

Determinations were made on the blood of a girl of 4 years 8 months, convalescent from infantile paralysis. These values are not included in any of the averages (Table 9). The sodium chlorid value is normal, that for blood solids much higher than the average for children.

Pneumonia. — Table 2 gives the results in four children with bronchopneumonia and in five children with lobar pneumonia, the ages

TABLE 2.—PNEUMONIA

Name	Date	Age, Months	Water in Blood, Per Cent. by Weight	Total Solids, Per Cent. by Weight	Chlorid in 1 C.c. Plasma Computed as Gm. of NaCl
BRONCHOPNEUMONIA					
Andrew N.	Oct. 10	15	82.05	17.95	0.00500
Joseph W.	Oct. 10	20	85.81	14.19	0.00534
Josephine C.	Oct. 13	10	82.90	17.10	0.00545
Carl H.	Dec. 21	12	82.43	17.57	0.00456
Average			83.30	16.70	0.00509
LOBAR PNEUMONIA					
Thomas W.	Oct. 10	30	83.71	16.29	0.00538
Gertrude G.	Oct. 10	33	83.66	16.34	0.00432
Rosemary D.	Oct. 10	10	82.62	17.38	0.00485
Isabella S.	Oct. 10	12	85.02	14.98	0.00473
Thomas L.	Dec. 20	15	81.99	18.01	0.00583
Average			83.40	16.60	0.00502

ranging from 10 to 30 months. The averages in the two groups are almost identical, both for solids and blood chlorid. But little importance is to be attached to the average for blood solids in either group, because of the wide variation met with. The average for blood chlorid is distinctly below normal; but there are two values in each group which are nearly normal. In the pneumonia cases as well as in the group of normal children there seems to be no correspondence between the variations in the blood solids and those in the sodium chlorid of the plasma.

Tetany.—The blood of ten children suffering from tetany of mild or severe type was examined. The ages ranged from 7 to 17 months. The results are shown in Table 3. The first four cases reported were

TABLE 3.—TETANY

Name	Date	Age, Months	Water in Blood, Per Cent. by Weight	Total Solids, Per Cent. by Weight	Chlorid in 1 C.c. Plasma Computed as Gm. of NaCl
Ferdinand E.	Dec. 21	17	82.39	17.61	0.00468
Edwin C.	Jan. 20	12	82.61	17.39	0.00549
Peter G.	Jan. 23	12	81.35	18.65	0.00482
Marcus C.	Mar. 28	14	.....	.....	0.00533
Edith McM.	Mar. 19	15	81.51	18.49	0.00458
Edith McM.	Mar. 22	15	79.34	20.66	0.00503
Rose G.	Dec. 1	17	83.18	16.82	0.00510
George I.	Dec. 1	9	84.67	15.33	0.00582
Billie C.	Dec. 19	13	81.28	18.72	0.00494
Mary S.	Jan. 12	7	82.52	17.48	0.00501
Gladstone F.	Mar. 28	14	.....	.....	0.00545
Average			82.09	17.91	0.00512

children with mild or moderate types of tetany; the remaining six all showed well-marked symptoms. The values for blood solids generally are higher than in normal children. The chlorid average is much lower than the normal, with only four values which even approximate it. No regularity can be seen in the relation of blood solids to the chlorid in the plasma in children with tetany.

Marasmus.—Table 4 shows the results of examination of the blood of twenty-three children suffering either from marasmus or from pro-

TABLE 4.—MARASMUS AND INTESTINAL DISTURBANCE

Name	Date	Age, Months	Water in Blood, Per Cent. by Weight	Total Solids, Per Cent. by Weight	Chlorid in 1 C.c. Plasma Computed as Gm. of NaCl
Mary McG.	Sept. 30	6	83.26	16.74	0.00370
Mary McG.	Oct. 13	6	83.44	16.56	0.00540
Florence H.	Oct. 4	9	82.56	17.44	0.00519
Solomon B.	Oct. 4	12	83.02	16.98	.....
Agnes L.	Oct. 4	6	82.96	17.04	0.00500
Salvatore L.	Oct. 4	5*	83.77	16.23	0.00523
Martin C.	Oct. 4	8	81.88	18.12	0.00454
John L.	Oct. 4	9	82.73	17.27	0.00442
Walter K.	Oct. 4	6	83.50	16.50	0.00468
Thaddeus E.	Oct. 4	6	83.63	16.37	0.00503
Edith F.	Oct. 6	6	83.07	16.93	0.00447
George N.	Oct. 6	3	83.90	16.10	0.00508
Leonie W.	Oct. 10	8	83.10	16.90	0.00412
Henrietta F.	Oct. 10	8	82.12	17.88	0.00500
Alfred D.	Oct. 10	7	81.37	18.63	0.00476
Alfred D.	Oct. 26	8	82.11	17.89	0.00576
August S.	Oct. 13	6	82.50	17.50	0.00478
James T.	Oct. 13	48	83.62	16.38	0.00396
Grace D.	Oct. 13	8	83.90	16.10	0.00515
Anna E.	Oct. 13	8	83.45	16.55	0.00500
Mary T.	Sept. 30	9	82.25	17.75	0.00412
Mary T.	Oct. 6	9	83.15	16.85	0.00353
John A.	Oct. 6	6	81.40	18.60	0.00461
John A.	Oct. 13	6	83.86	16.14	0.00412
Albert H.	Oct. 24	12	81.21	18.79	0.00483
Minnie C.	Jan. 13	16	83.63	16.37	0.00545
Thomas S.	Jan. 25	3	83.90	16.10	0.00560
Average			83.94	17.06	0.00475

*Weeks.

longed intestinal disturbance. The ages ranged from 5 weeks to 4 years, but most of the children were under 1 year. The average for blood solids is slightly below the normal average; that for blood chlorid very much below the normal. The range of values for blood solids, however, is very similar to that found in normal children. In this group, also, no regularity can be seen in the correspondence of blood solids and blood chlorid.

Concentrated Blood.—Three children among those examined showed abnormally concentrated blood. All of them had previously suffered from gastro-enteritis. In one, the blood concentration appeared to be the result of a transfusion; another had suffered from a severe burn; a third was deeply cyanosed at the time the blood was taken. The first and second cases had very high hemoglobin, in both instances reaching 140 per cent. The findings in these children are reported as a separate group in Table 5. Two examinations were made

TABLE 5.—Concentrated Blood

Name	Date	Age, Month	Water in Blood, Per Cent. by Weight	Total Solids, Per Cent. by Weight	Chlorid in 1 C.c. Plasma Computed as Gm. of NaCl	Hemoglobin, Per Cent.
Bernard K.	Oct. 6	8	80.34	19.66	0.00318	...
William C.	Oct. 4	1	77.12	22.88	0.00541	140
William C.	Oct. 13	1½	76.25	23.75	0.00412	140
Richard D.	Oct. 4	5½	80.37	19.63	.....	140
Richard D.	Oct. 13	6	79.20	20.80	0.00536	
Average			78.66	21.34		

of the blood of each of the children with high hemoglobin. The five values given for blood solids show a wide range, but are all in a totally different class from those of all the other children studied. These values approximate the values for normal adults. The chlorid values vary so greatly that an average of the four would have little significance. It is worth noting that one extremely low value is found in a child who had received, on the preceding day, a large subcutaneous injection of bicarbonate of soda and more of the same drug by mouth.

Nutritional Edema.—In Table 6 are given the results of eleven determinations of blood solids and blood chlorid in five children suffering from nutritional edema. The ages ranged from 2 months to 2 years. The findings in this group show a strikingly low average for blood solids. In not a single instance is the value as high as the average given for normal children, and in only one is the value as high as the lowest in the normal group. The values for blood chlorid do not differ greatly from the values found in the other pathologic groups, the average being much below normal. The range, however, is wide, including several approximately normal figures.

TABLE 6.—Nutritional Edema

Name	Date	Age, Months	Water in Blood, Per Cent. by Weight	Total Solids, Per Cent. by Weight	Chlorid in 1 C.c. Plasma Computed as Gm. of NaCl
Seraphine C.	Sept. 30	24	86.28	13.72	0.00437
Seraphine C.	Oct. 13	..	84.93	15.07	0.00511
Seraphine C.	Nov. 14	..	85.51	14.49	0.00590
Mathilda F.	Sept. 26	15	85.21	14.79	0.00417
Mathilda F.	Oct. 4	..	83.53	16.47	0.00511
Mathilda F.	Oct. 13	..	84.70	15.30	0.00511
Mary F.	Oct. 10	3	87.30	12.70	0.00468
Mary F.	Oct. 14	..	87.09	12.91	0.00550
Louise S.	Oct. 30	4	84.92	15.08	0.00536
Louise S.	Nov. 6	..	.....	.....	0.00445
Marie K.	Jan. 20	31	87.29	12.71	0.00510
Average			85.68	14.32	0.00499

Sclerema.—Three children, aged 2 months, 4 months and 2 months, respectively, having sclerema, were examined. The results are given in Table 7. The average for blood solids in this group is somewhat below normal, but does not at all resemble that obtained in the group of nutritional edema. Blood chlorid in two of the cases is normal, in the third it is extremely low. An injection of bicarbonate of soda had been given to this child on the previous day.

TABLE 7.—SCLEREMA

Name	Date	Age, Months	Water in Blood, Per Cent. by Weight	Total Solids, Per Cent. by Weight	Chlorid in 1 C.c. Plasma Computed as Gm. of NaCl
James V.	Oct. 14	2	83.73	16.27	0.00274
George K.	Oct. 28	2	83.48	16.52	0.00575
Nathaniel D.	Oct. 31	4	83.23	16.77	0.00644
Average			83.48	16.52	0.00498

After Bicarbonate Injection.—During the investigation three children in all had received subcutaneously a bicarbonate of soda injection within the twenty-four hours preceding the blood examination. The findings are grouped together in Table 8. The sodium bicarbonate

TABLE 8.—AFTER INJECTION OF SODIUM BICARBONATE

Name	Date	Age, Months	Injection	Water in Blood, Per Cent. by Weight	Total Solids, Per Cent. by Weight	Chlorid in 1 c.c. Plasma Computed as Gm. of NaCl
John A.	Oct. 13	6	Oct. 11—120 c.c.	83.86	16.14	0.00412
Bernard K...	Oct. 6	8	Oct. 5—240 c.c.	80.34	19.66	0.00318
James V. ...	Oct. 14	2	Oct. 13—120 c.c.	83.73	16.27	0.00274

injection may possibly have been the cause of the extremely low values here seen for chlorid in the plasma, but, on the other hand, several other children, in the marasmus and intestinal disturbance group, who had not received such an injection show similarly low values. In this connection a recent communication by K. Goto,[5] on blood studies in uranium nephritis in the dog and the protective action of sodium bicarbonate, is of interest. He finds that the increase of chlorid in the plasma observed in uranium nephritis is not so great when sodium bicarbonate is administered at the time.

After Saline Injection.—In ten children a physiologic salt solution had been injected subcutaneously shortly before the blood was studied. Although most of these findings have been included in the preceding tables, particularly that of the marasmus cases, they are presented together in Table 9. In two children the blood was examined shortly

TABLE 9.—AFTER INJECTION OF PHYSIOLOGIC SALT SOLUTION

Name	Date	Age, Months	Injection	Water in Blood, Per Cent. by Weight	Total Solids, Per Cent. by Weight	Chlorid in 1 c.c. Plasma Computed as Gm. of NaCl
Salvatore L..	Oct. 4	1	Oct. 3— 90 c.c.	83.77	16.23	0.00523
John L.	Oct. 4	9	Oct. 3—120 c..c	82.73	17.27	0.00442
Thaddeus E..	Oct. 4	7	Oct. 3—120 c.c.	83.63	16.37	0.00503
Grace D.....	Oct. 13	8	Oct. 12—240 c.c.	83.90	16.10	0.00515
John A.	Oct. 6	6	Oct. 5—120 c.c.	81.40	18.60	0.00461
Seraphine C.	Nov. 6	25	Nov. 5—240 c.c.	84.42	15.58	0.00618
Mary McG...	Oct. 4	6	Oct. 2—240 c.c.	82.69	17.31	0.00626
Nathaniel D..	Oct. 31	4	Oct. 30—120 c.c.	83.23	16.77	0.00644
Alfred D....	Oct. 26	8	Before injection	(82.11)	(17.89)	(0.00576)
Alfred D. ..	Oct. 26	8	Oct. 26—240 c.c.	.....	.....	0.00583
Albert H. ..	Oct. 24	12	Before injection	(81.21)	(18.79)	(0.00483)
Albert H. ..	Oct. 24	12	Oct. 24—240 c.c.	83.16	16.84	0.00539
Average				83.21	16.79	0.00545

5. Goto K.: Jour. Exper. Med., 1917, **25,** 693.

before and again a few hours after the hypodermoclysis. All these children show a somewhat lowered average for blood solids, but it is not lower than the values found for several children in the normal group, and it is very near the average found in the pneumonia and the sclerema groups. The average for chlorid in the plasma after saline hypodermoclysis is approximately normal. Since all the children who received hypodermoclysis belonged to the abnormal groups, in which blood chlorid is invariably lower, it seems evident that the injection of the saline raises the chlorid content of the plasma. Of the two children whose blood chlorid values before the hypodermoclysis were obtained, the one who showed a normal value before, showed practically no change after the injection; while the one who was below normal before the injection was brought almost to normal by it.

It is difficult to draw any definite conclusions as to the effect of diarrhea on the blood solids and chlorid. Nearly all the children with marasmus or intestinal disturbance had had more or less diarrhea. It might be expected that the blood water would be reduced, but this does not seem to be regularly the case. This group shows the lowest average found for blood chlorid. Except two cases in which soda bicarbonate had been injected, this group also includes all the very low values found.

An examination of Table 10 shows how great the tendency is for blood solids to remain constant. Only two groups show any significant

TABLE 10.—SUMMARY OF TABLES

	Water in Blood, Per Cent. by Weight, Average	Total Solids, Per Cent. by Weight		Chlorid in 1 c.c. Plasma Computed as Gm. of NaCl	
		Range	Average	Range	Average
Gettler and Baker, adults.....	77.6	20.0 –24.9	22.4	0.00500–0.00637	0.00592
Normal infants	82.61	16.23–18.27	17.39	0.00536–0.00641	0.00587
Infants with pneumonia	83.35	14.19–18.01	16.65	0.00432–0.00583	0.00505
Infants with tetany	82.09	15.33–18.72	17.91	0.00458–0.00582	0.00512
Infants with marasmus, etc...	82.94	16.10–18.63	17.06	0.00353–0.00576	0.00475
Infants with concentrated blood	78.66	19.63–23.75	21.34	0.00318–0.00541	0.00452
Infants with nutritional edema.	85.68	12.70–16.47	14.32	0.00437–0.00590	0.00499
Infants with sclerema	83.48	16.27–16.77	16.52	0.00274–0.00644	0.00498
Child, 4 yrs. 8 mos., convalescent from infantile paralysis.....	80.85	.....	19.15	.....	0.00594

variations from the normal. The children with nutritional edema seem to have a greatly diluted blood, while those with abnormally high hemoglobin have a greatly concentrated blood. All the other pathologic groups show blood solids not greatly different from the normal values for infants.

The most striking point brought out by this investigation is the fact that almost all children not in a normal condition have a remarkably low value for chlorid in the plasma. Only one of the normal children shows a value as low as most of the high values of the other groups. This child, H. R., though perfectly normal at the time of

examination, had suffered a year before from severe marasmus. Of the children in the pathologic groups that show values as high as normal, most had received a saline injection during the twenty-four hours preceding. A few other exceptions to the rule are found in some particularly well-nourished children in the pneumonia and tetany groups. It must be emphasized, however, that on the whole chlorid in the plasma is extremely low in children not in normal condition, especially if they are poorly nourished and suffering from digestive disturbances.

CONCLUSIONS

1. The normal infants studied had about the same concentration of chlorid in the plasma as normal adults; the average for total solids in the blood was about 5 per cent. lower in infants than in adults.

2. In pneumonia there was irregularity in the values found, both for total solids and chlorid in the plasma, which is difficult to account for.

3. Children suffering from tetany showed a tendency to slightly higher total solids and higher chlorid in the plasma than was found in any of the other pathologic conditions studied.

4. Children suffering from malnutrition and digestive disorders showed the lowest chlorid in the plasma of all those investigated.

5. Children with nutritional edema all showed abnormally dilute blood, with chlorid in the plasma much below normal, though not lower than that of other sick infants.

6. Infants with sclerema had nearly normal total solids in the blood, with chlorid in the plasma like that of the other pathologic cases, excepting the marasmus group.

7. There was no constant relation between the variations in total solids of the blood and those in chlorid of the plasma.

8. Saline hypodermoclysis seemed to affect the percentage of total solids very little, but to raise the chlorid in the plasma nearly to normal.

9. In general, all infants not in normal condition had low blood chlorid, frequently very much lower than normal, but, except in edema, or under some unusual condition of blood concentration, the percentage of the total solids in the blood of infants tended to remain constant.

RUMINATION IN THE FIRST YEAR OF LIFE*

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If one looks up the literature on rumination in infancy, he receives the impression that the condition is an extremely rare one, not only because of the paucity of reports, but also because of the extensive way in which single cases are treated, and the discussion of them.

So far as I have been able to find, the first mention of rumination in infancy, aside from the very cursory remarks in textbooks, is the report of Freund[1] in 1903. He speaks of a small number of cases of rumination, which he regards as closely related to pylorospasm. There is no definite report of single cases in his article. Since then there have appeared in the literature reports of cases by Maas,[2] Finkelstein,[3] Pouliot and Moricheau-Beauchant,[4] Wirtz,[5] Mayerhofer,[6] Sluka,[7] Lust,[8] Brüning,[9] Huldschinsky,[10] Aschenheim,[11] Lehnerdt,[12] Schippers,[13] Wanietschek,[14] and Strauch.[15] With the exception of Freund, we see that none of these has reported more than two cases. The number of cases observed by Freund is, of course, not definitely known. This represents a total of known cases of sixteen. The condition could hardly be overlooked after one's attention is called to it. It is so definitely characteristic, and so easily diagnosed, that errors in diagnosis should be extremely few. This, therefore, is not the reason why so few cases have been reported. The answer must be either that the cases are extremely rare, or else that they have not been recognized,

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1. Freund: Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1903, **11,** 325.
2. Maas: Med. Klin., 1907, **3,** 926.
3. Finkelstein: Lehrbuch der Saüglingskrankheiten, Berlin, 1908, II, Abt. I, p. 133.
4. Pouliot and Moricheau-Beauchant: Bull. Soc. de pédiat. de Paris, 1909, **11,** 88.
5. Wirtz: München. med. Wchnschr., 1910, **57,** 960.
6. Mayerhofer: Therap. Monatsh., 1912, **26,** 262.
7. Sluka: Wien. klin. Wchnschr., 1912, **25,** 288.
8. Lust: Monatschr. f. Kinderh., 1912, **10,** 317.
9. Brüning: Arch. f. Kinderh., 1913, **60,** 116.
10. Huldschinsky: Ztschr. f. Kinderh., 1913, **8,** 363.
11. Aschenheim: Ztschr. f. Kinderh., 1913, **8,** 161.
12. Lehnerdt: München. med. Wchnschr., 1914, **61,** 1977.
13. Schippers: Ztschr. f. Kinderh., 1914, **10,** 92.
14. Wanietschek: Jahrb. f. Kinderh., 1915, **82,** 66.
15. Strauch: Jour. Am. Med. Assn., 1915, **65,** 678.

because it would hardly seem from the literature that the cases were of such a nature as not to be worthy of special attention.

From the experience of the writer it would seem that the condition is much more frequent than is ordinarily supposed, and that the reason for not recognizing it is that the attention of the pediatric world in general has not been called to the condition in such a way as to bring it definitely before them. The following six cases, which were observed during a period of three years, one of which was previously reported by Strauch, constitute my reasons for believing that the condition is overlooked. It is desirable that this should not be the case, since rumination in infancy is an exceedingly fatal condition, and one about which we know extremely little. It is, therefore, desirable to be better informed on this subject, and to recognize all cases when they appear, in order to be in a position to study the condition more intensely and endeavor to arrive at some definite conclusions as to causation and treatment.

REPORT OF CASES

Case 1 (78293).—Christine B., aged 8 months, entered Presbyterian Hospital April 30, 1914. The present complaint was that the baby was unable to retain its food; took it readily, but soon began to vomit; had been slightly constipated. The child gained very little in weight. It was fed on breast milk up to three and one-half months, and was then weaned because the physician thought the milk probably did not agree with the child. Feeding, on entrance, consisted, in the twenty-four hours, of 10 ounces of whole milk, 6 ounces of gruel, 1¾ teaspoonfuls of magnesium citrate. It had never been sick before, except for a slight cold, and the family history was negative.

Aside from extreme emaciation, the examination showed nothing. On entrance the child weighed 8 pounds 3½ ounces. She was put on an albumin milk mixture, which was gradually increased up to May 24. During that time her temperature tended to be definitely subnormal, at times going as low as 97 F. During her entire stay at the hospital she regurgitated in a peculiar way. The milk was brought up into the mouth, often following sucking of the fingers. It was held there and gargled, usually a considerable amount of food being spilled out. This was done after every feeding, sometimes a few minutes, sometimes longer. The treatment consisted, first, of strychnin, 1/500 grain hypodermatically, four times a day, until May 4. Gastric lavage was given from May 2 to May 11, with apparently no benefit. From May 4 until May 24, bromids were given without effect. During this period on albumin milk feeding, the child showed a weight which was practically stationary, May 24 having a weight of 7 pounds 15½ ounces, a loss of 4 ounces in twenty-five days. The food was then changed to a modified albumin milk, which was thickened with flourball. This was continued until June 4 without any apparent effect on the child's health. Water, during this time, was supplied by means of continuous normal salt enemas, up to May 31. From May 28 strychnin was given, and June 3 bromids were again given. June 4 the child's weight was 7 pounds 14½ ounces. The change of food had apparently had no effect on the rumination. In fact, from June 4 there was a rapid decline in weight, so that on June 9 the infant weighed only 7 pounds 1 ounce, at which time the child left the hospital. Nothing further was heard of the patient. At no time was increased peristalsis noted.

Case 2 (79139).—Caroline D., aged 4 months, was brought to the hospital by her mother June 8, 1914, because she failed to gain in weight. The child

weighed practically the same as when she was born. From a few days after birth she had been fed every two hours with diluted milk, proportions unknown. Appetite good. She had vomited but little. Vomiting had not been a marked feature of the trouble. She always showed a tendency to constipation, so that it was necessary to give laxatives, and usually magnesium citrate was added to the food. The child was very restless and slept poorly. She was a full term child and the birth was normal. Examination showed a child considerably underweight, very fretful, but apparently not very sick. No palpable glands; throat was negative; heart and lungs negative; abdomen negative, as w e the extremities. July 21 she was first noticed to ruminate, which occurred several times in succession. This was only noted on one or two occasions, and immediately cleared up. Later, the child developed a pyelocystitis of moderate degree, and on August 5 a slight prolapse of the rectum. She left the hospital September 15, without showing any other signs of rumination. No increased gastric peristalsis was noted.

In this case the first rumination was noticed July 21. Thereafter this occurred not more frequently than once a day, and rarely that often. No rumination was noted after August 4.

Case 3 (83073).—Liebe S., aged 13 weeks, previously reported by Dr. Strauch.[13]

Case 4 (98449).—Kasmera S., aged 7 months, entered the Presbyterian Hospital Oct. 2, 1916, because of vomiting and loss of weight. The birth was normal, the birth weight was unknown. The child nursed at the breast for four and one-half months, every two hours or oftener, and was taken off the breast because the physician said the food did not agree with the child. The child was then put on Horlick's malted milk, 3 teaspoonfuls to 4 ounces of water every three hours, with which it was fed for one month. It was then put on condensed milk, half milk and half water, 4 ounces every three hours. To this 4 ounces was added ½ teaspoonful of sugar. The child vomited a little at every feeding while on the breast, but during the month previous to entrance, the mother thought that the child had vomited almost the entire feeding. During the summer, which was exceedingly hot, the child had had an attack of diarrhea, with fifteen green mucous stools a day. The father and mother are living and well. One other child is well. No miscarriages. On examination there was noted a greatly emaciated child, with the skin hanging loose. On first examination, definite signs of rumination were noted. In the neck there was a slight adenopathy. The chest and lungs were all right; there were a few palpable axillary glands; abdomen distended, especially in the epigastrium; intestines slightly distended. The liver was at the border of the ribs; the spleen was not palpable. Aside from emaciation, the extremities were negative. The child was put on albumin milk during its stay in the hospital, which was until October 14. During this time the temperature showed a marked tendency to be subnormal, averaging between 97 and 98 F. On entrance the weight was 7 pounds 2 ounces, which on October 13 had dropped to 6 pounds 14 ounces, and on the 14th, or day of death, the child's weight had risen to 7 pounds 5½ ounces.

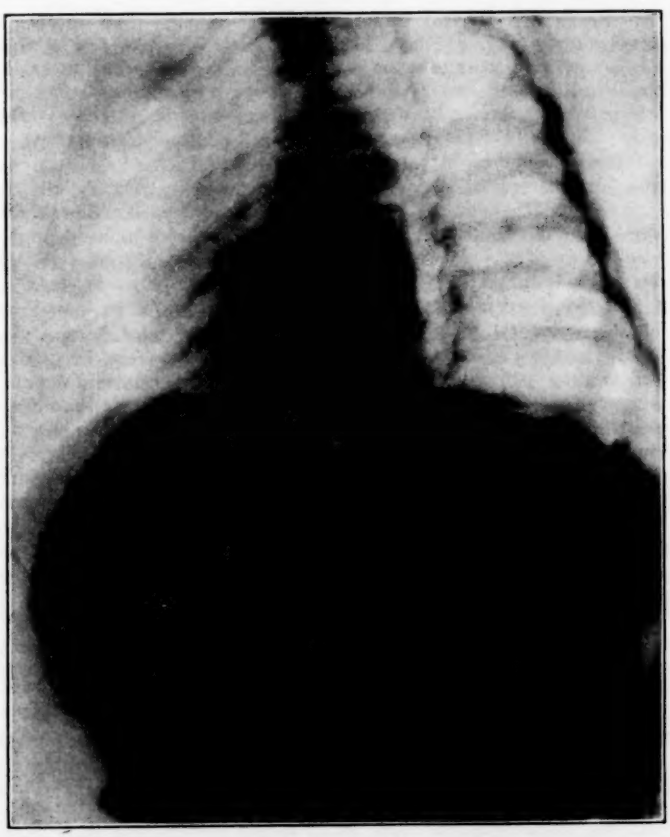
In this child, with the change of food, the treatment of Strauch of plugging the nostrils was tried faithfully, but seemed to have no effect whatever on the rumination, which was very severe, occurred after every feeding, and resulted in the expulsion of a large amount of the food taken in. Gastric lavage seemed to have no effect. The blood and urine showed nothing special. Roentgen-ray examination showed dilatation of the lower end of the esophagus (see illustration).

It was possible in this case to get only a partial necropsy. Such as it was, the report is as follows:

The stomach was found to have an exceptionally large fundus. The pyloric half was very small and narrow. The cardia was 2.5 cm. wide; 3 cm. above the cardia, 2.3 cm. wide. It was 8 cm. from the cardia to the pylorus. The

tip of the fundus was 5 cm. from the cardia, and it was 11 cm. from the tip of the fundus to the pylorus. Absolutely no cardiac sphincter muscle could be made out on gross examination. The pyloric sphincter was normal.

Microscopic examination of the stomach showed that the mucosa was intact throughout all the sections and presented no changes other than early post-mortem digestion. In sections taken from the cardia, the fundus and the pyloric portion, the arrangement and thickness of the musculature appeared normal (Raulston).



Roentgenogram of patient, Case 4, showing dilatation of the lower end of the esophagus.

CASE 5.—Baby C., aged 5 months, was seen by me March 9, 1915, in consultation with Dr. Renaud. The history was as follows: The child was born at full term; normal delivery; weight at birth, 10 pounds. It was nursed at the breast for three months. For the previous two months it had been given malted milk and cow's milk, with sugar and water. The child was first noticed to vomit on March 1. The vomited matter had been the food which the child had taken. There had been a definite tendency toward bringing the food up into the throat, holding it there a while, spilling over, and then swallowing again; in other words, a definite history of rumination. In the beginning of the vomiting, the child had lost rather rapidly, but had not been weighed at

the time of consultation, so it is not known how much the loss in weight had been. There had been no previous diseases, except a slight cold. There were no brothers or sisters. There was a slight neurotic tendency on the father's side. The mother was rather nervous.

On examination, an emaciated child was seen, very cross and quite easily disturbed. After taking food it was noticed that the food was brought up into the mouth, gargled for a short time, some of it spilling over, and then swallowed. This was repeated rather frequently. No gastric peristalsis was noted at this time, nor later, as reported by Dr. Renaud.

The diagnosis of rumination was made, and I suggested the treatment of Strauch by means of plugging the nostrils. This was not carried out, but after determining the nature of the disease, two other measures were followed: Immediately after the taking of food, when the child would start to regurgitate, its attention was attracted for some fifteen to twenty minutes, after which it was left alone; to do this, a little bell was rung, or some such procedure was resorted to. The child was given ⅛ grain chlorbutanol (chloretone) and 5 grains stronthium bromid every two to three hours.

According to the report, the child gained in weight quite rapidly, and on March 25 weighed 12½ pounds and rumination had ceased. The child after a year had shown no tendency to return to its former condition, and was a perfectly well, normal child, walking around and doing such things as any other child of its age should do.

Case 6 (10223).—Mary K., aged 7 months, entered the Presbyterian Hospital in the care of Dr. Winnolt Feb. 9, 1917. The history was that she had shown an inability to gain weight; some vomiting; frequent green curdy stools. She was a full term baby, vertex presentation, normal labor; birth weight, 8¼ pounds. For the first three months the infant gained weight steadily and then remained stationary. She had always vomited. She vomited not only immediately after nursing, but also at intervals up to the time of the next feeding. Occasionally this vomiting was projectile, but this was only once in awhile. For the first five months she was fed on breast milk entirely. Up to three months the breast had been given every three hours, then the interval had been lengthened to four hours, with the idea of decreasing the vomiting. During the fifth month the milk supply began to grow low, and her weight remained stationary and the vomiting became, if anything, worse. At five months the bottle feeding was begun. At first skim milk and water, equal parts, 7 to 8 ounces every three hours, were given. At this time the breast milk suddenly gave out. For two weeks skim milk was given, then cream was added, but on the cream mixture the vomiting was worse, so that the cream was stopped. After this, dextrimaltose was added to the skim milk. At five months the weight was 12 pounds, the same as that at three months. Dextrimaltose was used for two weeks. After that, Mellin's food for two weeks. For awhile she did not seem to vomit on this, but very soon the vomiting commenced the same as previously. She was then given condensed milk, 3 teaspoonfuls to 7 ounces of water every three hours at first, and then every four hours, with the addition of albumin water twice a day, which was begun a week before entrance. She gained half a pound on this, but soon lost it again.

There was no history of severe colds, fevers, or coughs. As to the stools, usually when a new food was first given the stools were normal. Later they seemed to become curdy and often green. There had been no mucus in the stools just previous to entrance, but when the child was on the breast there had been a great deal. Stools had recently been about five a day. They had never been hard. The child slept well, and, as a rule, did not waken at night. There was one older child. There was no tuberculosis in the family, and there had been no miscarriages.

Physical Condition: The patient was seen to be a fairly well nourished female infant, but somewhat undersized and under weight. The eyes, ears, scalp, nose and mouth were normal; no generalized lymph adenopathy; epi-

trochlear glands not palpable. The lungs and heart showed nothing abnormal; liver and spleen not palpable, nor was there any palpable mass in the abdomen; no visible gastric peristalsis. The weight on entrance was 11 pounds 12 ounces.

The child was put on a feeding of albumin milk, 35 ounces; cane sugar, ¾ ounces; malt extract, ¼ ounce; water, 7 ounces—six feedings of 7 ounces each. There was slight variation of this diet, the change being mostly in the shift from cane sugar to dextrimaltose, and an increase of the malt extract. Final feeding, albumin milk, 36 ounces; dextrimaltose, ¼ ounce; malt extract, ¾ ounce; barley water, 6 ounces—six feedings of 7 ounces each.

The temperature during the infant's stay in the hospital was within normal limits, except for a short period from February 22 to 26, when the child had an acute coryza. On entrance the blood showed: red blood cells, 4,530,000; whites, 7,900; hemoglobin, 75 per cent. There was a slight leukocytosis of 12,500 during the acute coryza. The urine throughout was negative. On February 12 it was first noticed that the child regurgitated some material into the mouth, which process was preceded by a sucking movement. After a few moments the child would swallow and the material would be regurgitated. On the 13th the child showed a very definite rumination at 8:30 in the evening. This lasted for about five minutes. On the 14th rumination was again seen, and this time the stomach was seen to assume a definite shape, and there were a few slight peristaltic movements. This rumination was noticed not oftener than twice a day, and continued, gradually decreasing in frequency, the last being noted February 19. On March 16 the weight was 12 pounds 14½ ounces, a gain since February 9 of 1 pound 2½ ounces.

We have, then, a case of a slight degree of malnutrition, accompanied by a rumination of not very great severity. This rumination, without any further treatment than a proper regulation of diet, gradually disappeared and had not returned over a period of practically a month. During a stay of five weeks in the hospital the child gained over a pound in weight, and in every way was in satisfactory condition.

DISCUSSION

In the cases found and reported by me, certain phenomena have seemed to be suspiciously common. The first of these is ulcer of the duodenum. This can probably be explained on the basis of an ulcer, due, as Helmholz[16] has already mentioned, to a streptococcus infection in a very depleted individual. It is altogether likely that the frequent presence of duodenal ulcer in these cases is not in itself of any etiologic importance, but rather is a complication or sequel of the condition. Of quite a different nature is the picture of pylorospasm. This has been described in too large a proportion of cases to be overlooked. It occurred in the cases of Lust, Case 2 of Aschenheim, and in that of Strauch. When we consider that the condition is perhaps not noted in a fair proportion of cases, we can regard this as a rather large percentage. Whether there is any connection between the definite tendency to increased muscular action of the stomach and the relatively decreased resistance of the cardia, is yet to be determined. The Roentgenogram accompanying Case 4 of this series shows a very definite dilatation of the esophagus of a spindle-shaped character, just above the cardiac orifice of the stomach. So far as I have been able to find,

16. Gerdine and Helmholz: Am. Jour. Dis. Child., 1915, **10**, 397.

this has not been reported before in infants. This is almost exactly similar to the condition which we find in cardiospasm, which Sippy has already pointed out. In cardiospasm in adults, the constriction does not occur at the cardiac orifice of the stomach, but just above it. This would seem to be the case in this instance. Most authors have been satisfied with the statement that the condition is a motor neurosis of the stomach. This hardly classifies rumination, nor distinguishes it from pylorospasm. We would expect, if it were only a motor neurosis of the stomach, that the reactions would remain in the stomach itself, but as we see, from the one case reported here, there is definite relaxation of the wall of the esophagus, with resultant dilatation. It seems to me that the whole condition would be best explained on the hypothesis of Hess[17] that the circular involuntary muscles all have a tendency to spasm in certain individuals, and that pylorospasm is only one isolated condition with which many others may be and often are associated. If the primary condition were a pylorospasm, the food after being forced back through the cardiac orifice might, through its irritation of the esophageal mucous membrane, produce a constriction in the lower end of the esophagus, with the result that the food is held in the esophagus, and that the gargling movements of the child result. As all of us know, overaction of the stomach musculature is not necessarily accompanied by visible gastric peristalsis. In fact, gastric peristalsis is only of significance when it is definitely visible, and is accompanied by vomiting, projectile in type. It would, therefore, seem to me that an hypothesis which would cover the needs in this instance would rest on a general tendency toward overaction of the involuntary circular muscles, with the primary action in the stomach from a pylorospasm (the term being used in the wide sense), the food then being forced back into the esophagus, the cardiac orifice of the stomach being closed by the overaction of the muscles of the lower end of the esophagus, with rumination resulting, rumination ceasing when these muscles have relaxed.

SYMPTOMATOLOGY

In general, we may divide these cases into two types, the mild and the severe. We will probably find cases which vary in severity, so that any hard and fast line may not be drawn between these two. In the mild type the rumination occurs only at long intervals, perhaps once or twice a day, and then is not so marked as to be accompanied by any definite loss of food. This condition usually responds readily to proper hygiene and feeding, and causes very little anxiety. Far different, however, is the severe case. Here we find a nervous, emaciated, pale

17. Hess: Am. Jour. Dis. Child., 1914, **7**, 184.

child, which cries rather easily and does not sleep well. The food which is given the child is well taken; in fact, greedily taken, and as a rule the stools show no special variation from the normal. Soon after the bottle is taken, the child begins to bring the food up. The food when brought into the mouth is gargled for a short time and then swallowed. This may happen again and again, the interval between the attacks being exceedingly short. The probable danger in this process is not in the process itself, but in the resultant loss of food through spilling over. In this condition an exceedingly large proportion of the food may be lost, so large a proportion, in fact, that the remainder may be, and frequently is, insufficient to support life. These attacks may occur at any time between feedings, and have been recorded by Schippers as occurring even during sleep. A very large proportion of these children die. Of those reported, the patients of Finkelstein, Lust, Lehnerdt and Strauch died. This, together with my Case 4, makes a mortality of almost 25 per cent.

As to the fate of many of the cases, we are doubtful, because they were not followed long enough; as, for instance, Case 1, reported in this series. Of the severer cases, certainly more than 25 per cent. of the infants die; probably as many as 50 per cent. die.

Aside from the symptoms of rumination, the children bear very great resemblance to severe cases of pylorospasm or of marasmus.

TREATMENT

The treatment as projected has been principally along three lines:

1. Drug treatment. This has consisted in giving bromids and other sedatives for this condition, and in using cocain and local anesthetics on the stomach. It may be said that there is no reason to think that such drug treatment will be successful in any great number of cases.

2. Dietetic. This has consisted largely in giving the child a thick vegetable puree or cereal gruel. In a few cases this has seemed to be of value, but in many it has utterly failed.

Strauch has suggested that the nostrils be plugged with wax in order to stop breathing, and thus reduce the tendency to rumination. This does not seem a logical procedure to us, and after having tried it in two cases we have abandoned it. In neither case did the plugging of the nostrils bring any result. In many cases washing of the stomach and introducing the food by means of a tube has been tried. This has been abandoned as not bringing definite results. It was tried in most of our cases with, apparently, no success.

3. I am inclined to feel that the idea of Schipper's is probably the best in regard to these cases, and that is the treatment of the psychic condition of the child. All unnecessary excitement should be avoided,

the child should be screened from its immediate surroundings, but immediately after taking food it would be well to draw its attention to some object, such, for instance, as a small bell or some plaything, to keep it absolutely distracted from any thought concerning the rumination. It seemed to me that this, more than anything else, was the cause of the ready response to treatment in Case 5.

CONCLUSIONS

1. Rumination is probably a much more frequent condition than is ordinarily supposed.

2. The condition can be explained on the basis of a hyperexcitability of the involuntary muscles, as suggested by Hess.

3. Treatment to be successful should probably be based on attention to the psychic condition of the child.

GLIOSARCOMA IN AN INFANT OF SEVEN WEEKS, RESEMBLING HYDROCEPHALUS *

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History.—Simon K., 7 weeks old, was admitted to the Babies' Hospital Jan. 16, 1917; only child, of Russian parentage; family history negative; full term; normal labor; birth weight reported, 6 pounds, 5 ounces. Breast fed to date of admission.

When about 2 weeks old the parents first noticed that the head was enlarging more rapidly than normal. A little later the veins of the scalp began to be very prominent. Both of these symptoms had increased steadily up to date of admission. There had been frequent vomiting and rather loose stools. The child had not thrived, but had apparently been failing in nutrition.

Physical Examination.—On admission, the child was fairly well developed but wasted. Compared with the small body, the head was enormous. The general appearance of the patient was that of a child with a hydrocephalus. Measurements were:

Circumference of head	51 cm.
Circumference of chest	39 cm.
Circumference of abdomen	34 cm.
Length of body	52 cm.

The head was somewhat asymmetrical, there being a very great prominence in the left frontal region. The scalp was covered with a network of enormously dilated veins. The skin of the scalp was tense and shining, especially over the most prominent portion. The sutures were widely separated. There was slight internal strabismus and occasional nystagmus; conjunctivae were normal; the knee jerks were present and active; no evidence of paralysis. The cry was feeble; the color good. There were no other deformities, and the examination of the abdomen and thorax was negative.

Course.—During the next few days the head increased greatly in size. The rapidity of the growth can best be indicated by the child's weight; in spite of the steady wasting of the body, the weight increased 650 gm. during the nine days of observation. The urine was negative. A spinal puncture showed a fluid under increased pressure containing 120 cells per c.mm., 63 per cent. of these being polymorphonuclears and 37 per cent. lymphocytes; the globulin test was positive. The temperature was most of the time subnormal. Food was taken badly and the bowels were loose.

Over the frontal eminence the scalp became very tense and thinner, till on the eighth day a spontaneous rupture took place over this prominence, followed by a discharge of a considerable quantity of cerebrospinal fluid, the amount of which it was difficult to estimate, but it probably did not exceed 150 c.c. The opening in the scalp appeared about 9 cm. long. The rupture was followed by a protrusion of brain substance—a true hernia cerebri. The child grew steadily

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weaker and death occurred two days later from exhaustion. There were no convulsions.

Necropsy.—The head measured 48.5 cm. in circumference. There was a rupture in the scalp and dura through which protruded cranial contents forming a mass 8 by 5 cm. in size and weighing 145 gm. The cerebrospinal fluid was but slightly in excess—not over 90 c.c. being present. The dura showed many punctate hemorrhages. The brain showed marked asymmetry, the left hemi-

Gliosarcoma of the brain.

sphere being fully three times the size of the right. The tumor mass involved practically the entire left hemisphere; it was a soft, lobulated new growth containing in its substance many softened areas, many recent hemorrhages and yellow pigmented remains of old hemorrhages.

While removing the brain the protruding mass forming the hernia cerebri broke off. This made up only a small part of the tumor. The

tumor apparently grew from the floor of the lateral ventricle and increased in size until it was enveloped only by a thin shell of the compressed cortex which varied in thickness from 1 to 5 mm. It involved the left hemisphere only. In the right hemisphere the convolutions were markedly flattened from pressure and there was moderate distention of the lateral ventricle, but no new growth was present. The cerebellum was compressed to about one-half normal size. After removal the left hemisphere measured 19.5 by 14 by 3 cm.; the right, 10.5 by 8.5 by 7.5 cm.

A microscopic examination of the tumor by Dr. Martha Wollstein, pathologist to the hospital, showed it to be a gliosarcoma. A complete autopsy was made but the examination of the other organs showed no new growths or any other lesions having any relation to the cerebral condition.

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THE EFFECT OF COD LIVER OIL ON GROWTH IN A CASE OF "INTESTINAL INFANTILISM"*

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Greatly retarded growth, amounting to a condition of infantilism, is occasionally seen as a result of certain prolonged derangements of the functions of digestion, as well as a consequence of organic changes in these organs. The exact nature of the changes which bring about arrested growth in the first mentioned group of cases is as yet little understood, but it has generally been connected with disturbances in the metabolism of calcium, magnesium and phosphorus. Negative balances in these substances have repeatedly been found in children belonging to this class.

Because of the demonstrated effect of cod liver oil in increasing the retention of these inorganic salts in other conditions, particularly in rickets, it was determined to try its effect on the patient whose history is here reported, in whom the diagnosis of infantilism of intestinal origin was tentatively made.

REPORT OF CASE

History.—Elizabeth R., aged 8½ years, came first under observation Feb. 9, 1916; her condition may be described in a word as "infantile," her weight being but 29 pounds net and height 39⅛ inches, or that of an average child of about 3 years. She was the eldest of three children, the other two being normal and well developed, a sister of 6 years being 4 inches taller and 12 pounds heavier than the patient. The parents were healthy and lived in a suburban town in excellent surroundings. The child had always had the best of home care.

Early progress was quite normal. She was born at term, weighing 8 pounds; was nursed for twelve months and did very well; muscular development was average. Weaning was easy and feeding for the second year not at all difficult. In fact, up to nearly 2 years of age, except that her stools were much of the time very pale, her progress was considered satisfactory. The food given at that time was chiefly milk, about 50 ounces being taken daily in five meals; she was also given beef juice, eggs and orange juice.

Ever since she was 2 years old the child had suffered from digestive symptoms, though she had never had acute attacks either of diarrhea or dysentery. Occasional vomiting was present during the first two years, but after that time vomiting attacks became more frequent, recurring every few days, and very

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often she would vomit during the night. The stools were always pale and were reported large in proportion to the food taken; at times she was constipated, but much of the time the stools were reported "frothy" in character, but no blood and rarely much mucus was present. There was always much gas in the bowels. Abdominal distention had been an almost constant symptom and most of the time it was extreme.

The diet had been much restricted. From the end of the second year milk had been excluded, also green vegetables, soups, cereals and fruits. Until a few months before her visit she had been fed chiefly on rare meat, eggs, toast and butter and a large amount of potato. For the last few months small quantities of milk had been added to the diet. The appetite was usually fair, but she constantly craved highly seasoned food and such articles as onions, strawberries, ice cream, lemons, green corn, etc.

The child had never had any acute illness except an attack of grip a few weeks before. Her progress mentally had been nearly that of the average child. On the whole, the mother considered her condition as rather better for the preceding six or eight months than previously, the abdominal distention had been much less and the stools of better character, but vomiting still occurred about twice every week.

No records of the weights had been kept; the following were given by the mother from memory:

At 12 months, 19 pounds; 3 years, 24½ pounds; 4 years, 30 pounds; 8 years, 30½ pounds (her best weight).

There were also no records of her height, but the mother thought that for the preceding two or three years there had been little or no growth.

Physical Examination.—On examination she appeared physically like an average child of 3 or 3½ years. The body was thin, but was in no sense wasted. The child was symmetrically small—trunk, face and extremities. The head was well formed and showed no irregularities or abnormalities; fontanel closed. Hands and feet, legs and arms were quite normal; facial expression, intelligent; speech and mental development were like that of an average child of 6 or 7 years. Physical examination of heart and lungs was negative. The circulation was rather poor; extremities much of the time cold. In the abdomen were found no abnormal masses; there was no distention. The liver and spleen were not palpable. Superficial glands were slightly enlarged. The tongue was coated; the breath now, and usually, sweet; the temperature was normal. There was moderate beading of the ribs, and very slight epiphyseal enlargement, but no signs of active rickets were present. The teeth, twenty in number, were in poor condition; several were carious.

Measurements: Weight, 29 pounds net; height, 39⅛ inches; head, circumference, 19¼ inches; chest, circumference, 20 inches.

Though she had suffered almost constantly from digestive symptoms since 2 years old, there did not seem to be in the diet a sufficient explanation for the arrested growth.

Metabolism Observations.—February 27 the child entered the Babies' Hospital for metabolism observations. She was given the same diet in variety and amount which she had been taking for several weeks previously. Though the quantity of food was small, it was all she would take at the time. The diet was as follows:

Breakfast: One egg; 2 slices toast; 2 gm. butter; 2 gm. sugar; one-half gm. salt.

Dinner: Scraped beef, 60 gm.; 15 c.c. beef juice; one-half small baked potato; 120 c.c. milk; 2 gm. sugar; 1 gm. salt.

Supper: Toast, one-half slice; 120 c.c. milk; 2 Huntley & Palmer breakfast biscuits; 2 gm. butter; 2 gm. sugar.

Was given 60 c.c. water at each meal and all she would take between meals. Total calories in her food, 650.

Weight on beginning metabolism observations was 12.5 kilos (27½ pounds); she was thus receiving at this time but 52 calories per kilo.

In Table 1 are given the average daily intake and excretion for the three days of metabolism observations.

TABLE 1.—METABOLISM OBSERVATIONS, FIRST PERIOD—FEB. 23-26, 1916

	Grams, Daily Average								
	Nitrogen	Fat	CaO	MgO	P_2O_5	Cl	K_2O	Na_2O	Total Ash
Intake	5.8398	24.176	0.5049	0.1802	1.3052	1.4279	1.4438	0.8593	5.4532
Excreted in feces	0.7551	11.218	0.7043	0.1525	0.7219	0.0655	0.5075	0.0534	2.2425
Absorbed	5.0847	12.958	—0.1994	0.0277	0.5833	1.3624	0.9363	0.8059	3.2107
Excreted in urine	4.2200	.....	0.0181	0.0582	0.7149	1.2212	0.6523	1.0638	3.5802
Retained	+0.8647	12.958	—0.2175	—0.0305	—0.1316	+0.1412	+0.2840	—0.2579	—0.3695
Per cent. of intake retained	14.77	53.65	..... —43.1	..... —16.9	..... —10.1	9.88	19.7	..... —30.0	..... —6.77

Dried weight of feces, average daily, 18.53 gm.

On this restricted diet the child had relatively large, constipated, but well-digested, stools. The metabolism balances showed a fair nitrogen and fat retention, but a very striking loss in mineral salts, only potassium and chlorin showing a positive balance. The abnormal loss took place chiefly through the feces.

For how long a period such a disturbance of salt metabolism had existed it was of course impossible to say, but the negative balances found coincided with the clinical history of the case. Something which would aid in the absorption of salts, particularly calcium and phosphorus, or lessen their excretion through the intestine was evidently what was needed. Even though there were no evidences of active rickets, it was decided to try the effect of cod liver oil as soon as the condition of the digestive organs warranted it, and at the same time to increase the salt intake by giving more food, particularly more milk.

At the end of a month the mother reported that the child had vomited but twice, that she was eating much better and was now able to take besides her other food, 360 c.c. of milk daily. The bowels were now quite regular. Cod liver oil with maltine (a preparation containing 30 per cent. oil) was begun about April 1, 1 teaspoonful twice daily, the dose being gradually increased until at the end of a few weeks she was taking 2 teaspoonfuls three times daily, this being equivalent to about 8 c.c. of the pure oil daily. This amount was continued up to the end of August, a period of about five months. It was then omitted for two months.

In June, July and August she suffered from a moderate attack of whooping cough. During this period the appetite was poor, but she "took her food as a duty," the mother reported. In spite of these adverse conditions the gain in weight was steady, so that by the end of August she was 5 pounds above her low weight early in March. With the subsidence of the whooping cough the appetite returned and her gain in weight was now rapid. The net weights during the summer were as follows:

June 9, 31½ pounds; August 25, 32½ pounds; September 28, 36½ pounds; November 1, 40 pounds.

The diet was practically the same as that mentioned above, except that the milk had been increased to 500 c.c. daily. Much difficulty was experienced in making her take vegetables; the only one she would take was carrots.

The next opportunity for an examination of the child was on November 10. Her measurements were as follows:

Weight, 41¼ pounds; height, 41½ inches; head, circumference, 19¾ inches; chest, circumference, 22½ inches.

This represented a gain in nine months of 2⅜ inches in height and of 2½ inches in circumference of chest, and in weight of 13¾ pounds in eight and a half months. The improvement in the general condition was striking; though still very small, she was plump and well nourished; the tongue clean; the abdomen slightly distended; the circulation excellent. She was able to walk a mile a day.

For three weeks during the latter part of November, with an attack of bronchitis, the appetite was lost and her digestion was considerably upset; she vomited occasionally; the bowels became loose and the same light colored "foamy" stools previously mentioned returned. In this attack she lost nearly 4 pounds in weight.

December 12 she entered the hospital a second time for metabolism study; observations were continued for a three-day period, beginning December 15. Her weight on admission was 37 pounds 6 ounces. The body was well nourished; color good; child good natured and happy; very much more active than during her previous admission. Her stools were formed, in fact, rather constipated, a daily enema being required; they were of a grayish-yellow color, but well digested.

She continued on the same diet which she had been taking at home, which was as follows:

Breakfast: One egg on 1 piece of toast, thinly buttered; 200 c.c. milk; 1½ slices graham bread and butter.

Dinner: Graham bread, 1½ slices, with butter; 2 tablespoonfuls scraped beef; 1 small baked potato with 1 ounce beef juice; 200 c.c. milk.

Supper: One slice white and 1 slice graham bread with butter; 200 c.c. milk.

Two teaspoonfuls of cod liver oil with maltine were, as before, given after each meal. Total calories given estimated at 1,030, making 61 per kilo or 28 per pound.

The intake, excretion and balances for this metabolism period are given in Table 2.

TABLE 2.—METABOLISM OBSERVATIONS, SECOND PERIOD—DEC. 15-18, 1916

	Grams, Daily Average								
	Nitrogen	Fat	CaO	MgO	P_2O_5	Cl	K_2O	Na_2O	Total Ash
Intake	8.5701	43.382	1.3283	0.3821	2.6311	3.4650	2.3624	2.6159	11.9358
Excreted in feces	1.4090	14.642	1.0994	0.3163	0.7450	0.1586	0.5841	0.2560	3.5217
Absorbed	7.1611	28.740	0.2289	0.0661	1.8861	3.3264	1.7783	2.3599	8.4141
Excreted in urine	5.3390	.....	0.0174	0.0513	1.3950	2.7840	1.0312	2.1192	6.7092
Retained	1.8221	28.740	0.2115	0.0148	0.4911	0.5424	0.7471	0.2407	1.7049
Per cent. of intake retained	21.3	66.3	15.9	3.87	18.6	15.65	31.6	9.2	14.3

Dried weight of feces, average daily, 31.5 gm.

This showed, as compared with Table 1, a somewhat increased retention of nitrogen and fat; but the most striking changes were in the salt balances. Instead of a negative balance in total ash of 6.77 per cent., there was a positive balance of 14.3 per cent. All the salts showed positive balances. The most marked changes were in the calcium where a negative balance of 43.1 per cent. was changed to a positive balance of 15.9 per cent.

Six weeks after leaving the hospital, in spite of intercurrent varicella and a mild otitis, the mother reported that she had never known her in better health; she had regained her weight lost during the bronchitis. A report late in March stated that she was in excellent condition except slight stiffness of the legs (rheumatism?) which she had suffered from in previous cold seasons.

The effect of cod liver oil and phosphorus in increasing the calcium and phosphorus retention in rickets has been known for a number of years. The careful observations of E. Schloss,[1] Schabad,[2] Birk[3] and many others[4] have established this fact beyond question. It has been repeatedly noted in our own observations at the Babies' Hospital. In a recent case the figures for the per cent. of the intake of the different salts absorbed and retained were as follows:

	CaO		P_2O_5		K_2O	
	Absorbed	Retained	Absorbed	Retained	Absorbed	Retained
Before cod liver oil and phosphorus...	16.6	14.0	51.5	18.0	74.2	12.9
After cod liver oil and phosphorus...	45.1	43.8	88.3	33.0	87.3	23.8

The value of the phosphorus in the combination is questioned by Schloss, though Schabad considers it important. Exactly how it is that the cod liver oil acts, has not yet been clearly shown. It certainly creates conditions which allow the calcium intake to become incorporated into the organism.

From Schloss' observations it would seem to be essential that there should be ample intake of calcium in order to obtain benefit from the cod liver oil. He found, for instance, that with a rachitic breast-fed infant the administration of cod liver oil and phosphorus did not improve the condition; but that when calcium acetate was added great improvement followed. It is undoubtedly true that the intake may be low in some breast-fed infants; but it is almost always adequate in those who are artificially fed.

In a later communication, Schloss states that calcium-phosphorus preparations alone with breast feeding are almost as effective in improving the calcium and phosphorus balances as when they are used with cod liver oil. The simple inorganic salts, he believes, added to breast milk as a food, work better than the natural salts of cow's milk, even when cod liver oil is added. His conclusion is that the nature of the food and the condition of absorption in the body are of even more importance than the form of salt addition.

In the patient under consideration there were but slight evidences of old rickets and none whatever of any active rickets. The cod liver

1. Schloss, Ernst: Jahrb. f. Kinderh., 1913, **28,** 694.
2. Schabad, J. A.: Monatschr. f. Kinderh., 1911, **9,** 659; **10,** 12; 1912, **11,** 4.
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oil was administered with the hope, but without very much expectation, that it might influence salt retention. At the same time, by increasing the diet, especially the amount of milk, an attempt was made to increase the salt intake. The results in this case far exceeded our expectations and they showed conclusively how essential to proper growth is the assimilation of the salts ingested.

There are certainly several factors that must be considered in explaining the improvement in this patient. An improved digestion from the omission of certain disturbing articles of food, an enlarged diet, particularly the addition of the milk, the cod liver oil, and possibly the preparation of malt with which it was administered — any one or possibly all of these were factors in the result. It is our own belief that the cod liver oil was by far the most important one, the next being the milk.

Whether children like the one whose history is here given are likely to reach a normal physical development, is a question of great interest. We know from the studies of Osborne and Mendel on rats that growth may be arrested by deficient feeding for very long periods, and then by proper feeding, growth and development may be resumed until the normal is reached. They found, however, that there was a period beyond which, if the deficient feeding was continued, growth was not resumed. There are, then, certain limitations to growth which cannot be exceeded. All children like this one need to be closely watched, and, if possible, metabolism observations made from time to time to determine the result of the feeding.

PROGRESS IN PEDIATRICS

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